```
=> d his

     (FILE 'HOME' ENTERED AT 12:32:05 ON 04 NOV 2003)

     FILE 'REGISTRY' ENTERED AT 12:32:15 ON 04 NOV 2003
L1                STRUCTURE UPLOADED
L2                QUE L1
L3              7 S L2
L4           1344 S L2 SSS FUL

     FILE 'CAPLUS' ENTERED AT 12:34:24 ON 04 NOV 2003
L5            133 S L4

     FILE 'REGISTRY' ENTERED AT 12:36:05 ON 04 NOV 2003
L6                STRUCTURE UPLOADED
L7                QUE L6
L8                STRUCTURE UPLOADED
L9                QUE L8
L10           254 S L7  SUB=L4 FUL
L11           113 S L9  SUB=L4 FUL
L12           347 S L10 OR L11

     FILE 'CAPLUS' ENTERED AT 12:37:25 ON 04 NOV 2003
L13            64 S L12

     FILE 'REGISTRY' ENTERED AT 12:37:41 ON 04 NOV 2003
L14           692 S L4 AND NRS>2
L15           200 S L12 AND NRS>2
L16           147 S L12 NOT L15

     FILE 'CAPLUS' ENTERED AT 12:42:43 ON 04 NOV 2003
L17            39 S L15

=> d l2
L2 HAS NO ANSWERS
L1                STR
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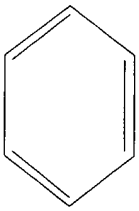

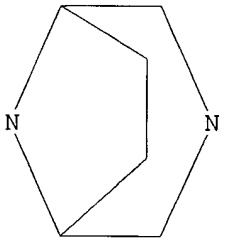


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Structure attributes must be viewed using STN Express query preparation.
L2                QUE  ABB=ON  PLU=ON  L1


=> d l7
L7 HAS NO ANSWERS
L6                STR
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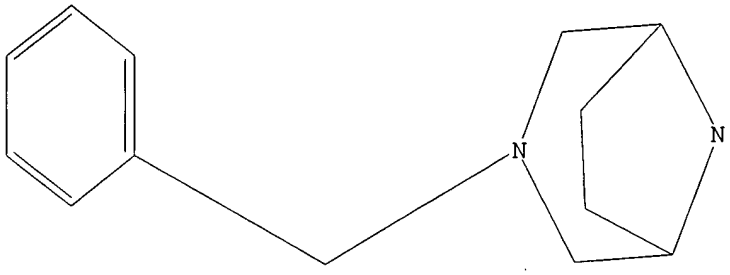
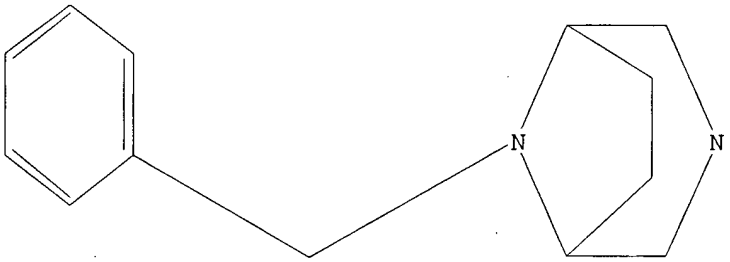


Structure attributes must be viewed using STN Express query preparation.
L7 QUE ABB=ON PLU=ON L6

=> d l9
L9 HAS NO ANSWERS
L8 STR



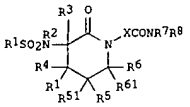
Structure attributes must be viewed using STN Express query preparation.
L9 QUE ABB=ON PLU=ON L8

=> d ibib abs hitstr 1-39 l17

L17 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:594840 CAPLUS
DOCUMENT NUMBER: 137:154858
TITLE: Preparation of arylsulfonamidopiperidones as inhibitors of Factor Xa.
INVENTOR(S): Stein, Philip P.; O'Connor, Stephen P.; Lawrence, R. Michael; Shi, Yan
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060894	A2	20020808	WO 2002-US2542	20020128
WO 2002060894	A3	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6555542	B1	20030429	US 2002-59621	20020129

PRIORITY APPLN. INFO.: US 2001-264964P P 20010130
OTHER SOURCE(S): MARPAT 137:154858
GI

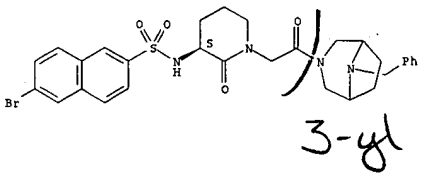


I

AB Title compds. [I; X = (substituted) (CH2)m; m = 1-3; R1 = (substituted) alkyl, alkenyl, alkynyl, aryl, heteroaryl, etc.; R2, R3 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, etc.; R4, R41, R5, R51 = H, OH, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, alkoxy, etc.; R6, R61 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, etc.; R7, R8 = (substituted) (CH2)nH; n = 1-4; R7R8N = (substituted) cycloheteroalkyl], were prepd. as cardiovascular agents (no data). 974 I, including (II), were prepd.
IT **445273-60-9P**

L17 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arylsulfonamidopiperidones as inhibitors of Factor Xa)
RN 445273-60-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[[(3S)-3-[[(6-bromo-2-naphthalenyl)sulfonyl]amino]-2-oxo-1-piperidinyl]acetyl]-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

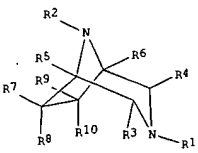


3-yl

L17 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:314941 CAPLUS
DOCUMENT NUMBER: 136:340701
TITLE: Preparation of 3,8-diazabicyclo[3.2.1]octanes for treating cardiac arrhythmias
INVENTOR(S): Bjoersne, Magnus; Hoffmann, Kurt-Juergen; Ponten, Fritiof; Strandlund, Gert; Svensson, Peder; Wilstermann, Michael
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032902	A1	20020425	WO 2001-SE2294	20011018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001096173	A5	20020429	AU 2001-96173	20011018
EP 1328526	A1	20030723	EP 2001-977023	20011018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: SE 2000-3795 A 20001020
WO 2001-SE2294 W 20011018
OTHER SOURCE(S): MARPAT 136:340701
GI

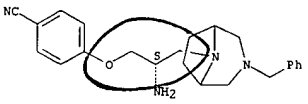


I

AB The title compds. [I; one of R1 and R2 = R1a and the other = ACR13R14BR15 (wherein R1a = alkyl optionally substituted and/or terminated by one or more groups selected from halo, CN, NO2, etc.; R13 = H, halo, alkyl, etc.; R13R14 = O; or R14 = H, alkyl; R15 = (un)substituted aryl, heteroaryl; A = alkylene, etc.; B = a bond, alkylene, etc.); R3-R10 = H, alkyl], useful in the prophylaxis and in the treatment of arrhythmias, in particular atrial and ventricular arrhythmias, were prepd. Thus, reacting tert-Bu

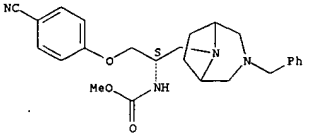
L17 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
3-(4-cyanophenoxy)-1-(3,8-diazabicyclo[3.2.1]oct-8-ylmethyl)propylcarbamate (prepn. given) with Bu isocyanate in the presence of Et3N in MeCN followed by treatment with HCl/EtOAc afforded I [R1 = CONHBu; R2 = CH2CHNH2CH2CH2O-p-C6H4CN; R3-R10 = H] in quant. yield. The exemplified compds. I showed pIC50 values of at least 5.5 for K channel blockade.
IT **415975-69-8P 415975-70-1P 415976-92-0P**
415977-56-9P 415977-64-9P 415977-72-9P
415977-80-9P 415977-86-5P 415977-95-6P
415978-02-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3,8-diazabicyclo[3.2.1]octanes for treating cardiac arrhythmias)
RN 415975-69-8 CAPLUS
CN Benzonitrile, 4-[(2S)-2-amino-3-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



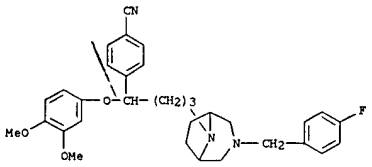
RN 415975-70-1 CAPLUS
CN Carbamic acid, [(1S)-1-[(4-cyanophenoxy)methyl]-2-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

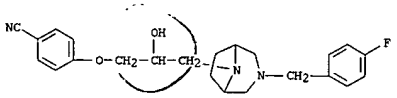


RN 415976-92-0 CAPLUS
CN Benzonitrile, 4-[1-(3,4-dimethoxyphenoxy)-4-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]butyl]- (9CI) (CA INDEX NAME)

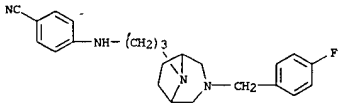
L17 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



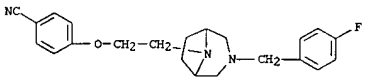
RN 415977-56-9 CAPLUS
CN Benzonitrile, 4-[3-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-hydroxypropoxy]- (9CI) (CA INDEX NAME)



RN 415977-64-9 CAPLUS
CN Benzonitrile, 4-[[3-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]propyl]amino]- (9CI) (CA INDEX NAME)



RN 415977-72-9 CAPLUS
CN Benzonitrile, 4-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]ethoxy]- (9CI) (CA INDEX NAME)

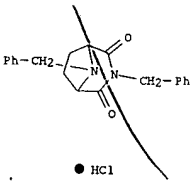


RN 415977-80-9 CAPLUS
CN Benzonitrile, 4-[[3-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]propyl]sulfonyl]- (9CI) (CA INDEX NAME)

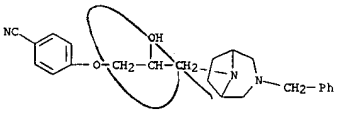
L17 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

IT **17740-41-9P 415979-11-2P 415979-13-4P**
415979-15-6P 415979-34-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3,8-diazabicyclo[3.2.1]octanes for treating cardiac arrhythmias)

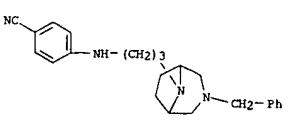
RN 17740-41-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 3,8-bis(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



RN 415979-11-2 CAPLUS
CN Benzonitrile, 4-[2-hydroxy-3-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]propoxy]- (9CI) (CA INDEX NAME)

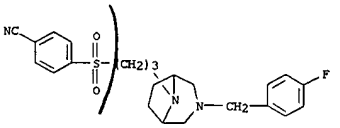


RN 415979-13-4 CAPLUS
CN Benzonitrile, 4-[[3-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]propyl]amino]- (9CI) (CA INDEX NAME)

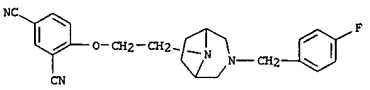


RN 415979-15-6 CAPLUS
CN Benzonitrile, 4-[1-(3,4-dimethoxyphenoxy)-4-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]butyl]- (9CI) (CA INDEX NAME)

L17 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

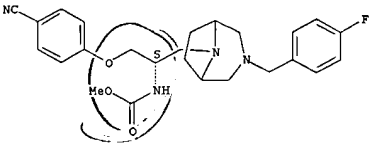


RN 415977-86-5 CAPLUS
CN 1,3-Benzenedicarbonitrile, 4-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]ethoxy]- (9CI) (CA INDEX NAME)

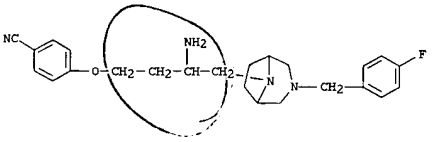


RN 415977-95-6 CAPLUS
CN Carbamic acid, [(1S)-2-(4-cyanophenoxy)-1-[[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]methyl]ethyl]-, methyl ester (9CI) (CA INDEX NAME)

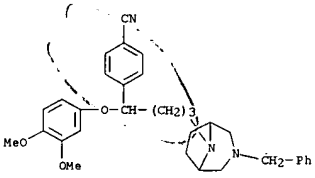
Absolute stereochemistry.



RN 415978-02-8 CAPLUS
CN Benzonitrile, 4-[3-amino-4-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]butoxy]- (9CI) (CA INDEX NAME)

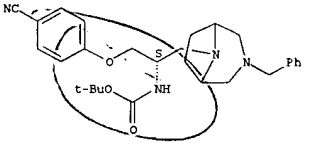


L17 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 415979-34-9 CAPLUS
CN Carbamic acid, [(1S)-1-[(4-cyanophenoxy)methyl]-2-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



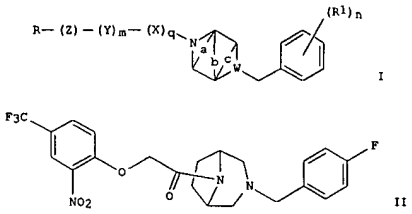
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:314940 CAPLUS
DOCUMENT NUMBER: 136:340711
TITLE: Bridged piperazine derivatives, specifically 3,8-diazabicyclo[3.2.1]octane, 8-azabicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, and 3,9-diazabicyclo[3.3.1]nonane derivatives, useful as inhibitors of chemokines binding to CCR1 receptors, for treating inflammation and other immune disorders.
INVENTOR(S): Blumberg, Laura Cook; Brown, Matthew Frank; Glaude, Ronald Paul; Poss, Christopher Stanley
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032901	A2	20020425	WO 2001-IB1844	20011004
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001092160	A5	20020429	AU 2001-92160	20011004
EP 1326867	A2	20030716	EP 2001-972389	20011004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002119961	A1	20020829	US 2001-972177	20011005
NO 2003001572	A	20030610	NO 2003-1572	20030408
PRIORITY APPLN. INFO.:			US 2000-241804P P	20001019
			WO 2001-IB1844 W	20011004

OTHER SOURCE(S): MARPAT 136:340711
GI

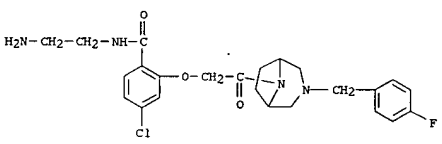


AB Compds. I and their pharmaceutically acceptable salts, useful for treatment of inflammation and other immune disorders, are disclosed [wherein: n = 1-5; m = 1-5; q = 0-1; a, b, c = (CH2)0-4 (independently); a, b, and c cannot all be null; if a and/or c is not null, then b must be null; W = CH or N; X = CO, C(S), or CH2; Y = CH2; Z = O, (un)substituted NH or (un)substituted CH2; R = certain (un)substituted (hetero)aryl or (hetero)cycloalkyl; R1 = (independently) H, OH, SO3H, halo, alkyl, SH, CF3, wide variety of other substituents]. The compds. are useful for treatment of a wide variety of diseases and disorders, which are cited specifically in claims. Approx. 100 specific examples of I are given, many with synthetic details. For example, 3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]octan-2-one (prepn. given) underwent a sequence of: (1) redn. of the amide carbonyl using LiAlH4 (94%); (2) 8-N-acylation with chloroacetyl chloride (69%); and (3) etherification with 2-nitro-4-trifluoromethylphenol (58%), to give title compd. II. In a bioassay for the ability to inhibit chemotaxis of various cells (THP-1 cells, primary human monocytes, or primary lymphocytes) in vitro, all example compds. had IC50 values of less than 10 .mu.M.

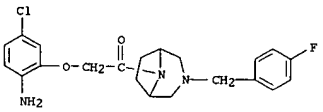
IT **417726-56-8P 417726-79-5P**, 2-(2-Amino-5-chlorophenoxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-83-1P**, 2-(3-Amino-5-chloropyridin-2-yloxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of bridged piperazine derivs. as inhibitors of chemokines binding to CCR1 receptors)

RN 417726-56-8 CAPLUS
CN Benzamide, N-(2-aminoethyl)-4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

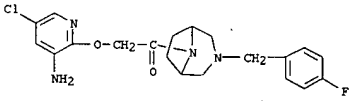
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-79-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[(2-amino-5-chlorophenoxy)acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 417726-83-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[(3-amino-5-chloro-2-pyridinyl)oxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



IT **417726-39-7P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-(2-nitro-4-trifluoromethylphenoxy)ethanone **417726-40-0P**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzamide **417726-41-1P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-(2-ethoxycarbonyl-4-chlorophenoxy)ethanone **417726-42-2P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-(2-acetyl-5-chlorophenoxy)ethanone **417726-43-3P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-(2-sulfamoyl-5-chlorophenoxy)ethanone **417726-44-4P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-(2-nitro-5-trifluoromethylphenoxy)ethanone **417726-45-5P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-[2-[(ethoxycarbonyl)methyl]-5-chlorophenoxy]ethanone **417726-46-6P**, 5-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]benzenesulfonamide **417726-47-7P**, 4-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]benzenesulfonamide **417726-48-8P**, 4-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]benzamide **417726-49-9P**,

L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

AB Compds. I and their pharmaceutically acceptable salts, useful for treatment of inflammation and other immune disorders, are disclosed [wherein: n = 1-5; m = 1-5; q = 0-1; a, b, c = (CH2)0-4 (independently); a, b, and c cannot all be null; if a and/or c is not null, then b must be null; W = CH or N; X = CO, C(S), or CH2; Y = CH2; Z = O, (un)substituted NH or (un)substituted CH2; R = certain (un)substituted (hetero)aryl or (hetero)cycloalkyl; R1 = (independently) H, OH, SO3H, halo, alkyl, SH, CF3, wide variety of other substituents]. The compds. are useful for treatment of a wide variety of diseases and disorders, which are cited specifically in claims. Approx. 100 specific examples of I are given, many with synthetic details. For example, 3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]octan-2-one (prepn. given) underwent a sequence of: (1) redn. of the amide carbonyl using LiAlH4 (94%); (2) 8-N-acylation with chloroacetyl chloride (69%); and (3) etherification with 2-nitro-4-trifluoromethylphenol (58%), to give title compd. II. In a bioassay for the ability to inhibit chemotaxis of various cells (THP-1 cells, primary human monocytes, or primary lymphocytes) in vitro, all example compds. had IC50 values of less than 10 .mu.M.

IT **417726-56-8P 417726-79-5P**, 2-(2-Amino-5-chlorophenoxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-83-1P**, 2-(3-Amino-5-chloropyridin-2-yloxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of bridged piperazine derivs. as inhibitors of chemokines binding to CCR1 receptors)

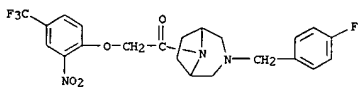
RN 417726-56-8 CAPLUS
CN Benzamide, N-(2-aminoethyl)-4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

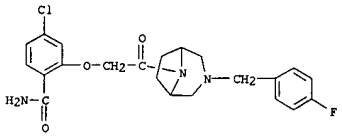
5-Methoxy-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]benzamide **417726-50-2P**, 4-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]-1-nitrobenzene **417726-51-3P**, 2-(5-Chloroquinolin-8-yloxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-52-4P**, 1-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-(6-methyl-2-nitropyridin-3-yloxy)ethanone **417726-53-5P**, 2-(5-Chloro-3-nitropyridin-2-yloxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-54-6P**, 2-(5-Chloro-3-carbamoylpyridin-2-yloxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-55-7P**, 2-(5-Chloro-3-methoxycarbonylpyridin-2-yloxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-57-9P**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid **417726-58-0P**, 4-Methyl-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid **417726-59-1P**, 4-Methoxy-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid **417726-60-4P**, 4-Iodo-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid **417726-61-5P**, 4-Bromo-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid **417726-62-6P**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzeneacetic acid **417726-63-7P**, 5-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]benzoic acid **417726-64-8P**, 5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]nicotinic acid **417726-65-9P**, 3-[2-[3-(4-Fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]naphthalene-2-carboxylic acid **417726-66-0P**, 4-Chloro-1-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]naphthalene-2-carboxylic acid **417726-67-1P**, 5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-(1H-tetrazol-5-yl)benzamide **417726-68-2P**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-(carboxymethyl)benzamide **417726-69-3P**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-(methanesulfonyl)benzamide **417726-70-6P**, 4-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]-N-(1H-tetrazol-5-yl)benzamide **417726-71-7P**, 4-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]-N-(carbamoylmethyl)benzamide **417726-72-8P**, N-Carbamoylmethyl-5-chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]nicotinamide **417726-73-9P**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-(2-ureidoethyl)benzamide **417726-74-0P**, 1-(5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl)-3-(carbamoylmethyl)urea **417726-75-1P**, N-[4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]urea **417726-76-2P**, 1-[4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]-3-(2-carboxyethyl)urea **417726-77-3P**, [5-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]phenyl]urea **417726-78-4P**, 2-[3-[5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]pyridin-3-yl]ureido]acetamide **417726-80-8P**, 2-(2-Amino-4-trifluoromethylphenoxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-81-9P**, 2-(2-Amino-4-chlorophenoxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-82-0P**, 2-(2-Amino-4-chlorophenoxy)-1-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]ethanone **417726-84-2P**, 2-(2-Amino-6-methylpyridin-3-yloxy)-1-[3-(4-fluorobenzyl)-3,8-

L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
diazabicyclo[3.2.1]oct-8-yl]ethanone **417726-85-3P**,
2-Amino-N-[5-chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]pyridin-3-yl]acetamide **417726-86-4P**,
N-[5-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]phenyl]-3-hydroxy-3-methylbutyramide **417726-87-5P**,
N-[4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]methanesulfonamide **417726-88-6P**,
N-[5-(Trifluoromethyl)-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]methanesulfonamide **417726-89-7P**,
N-[5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]methanesulfonamide **417726-90-0P**,
N-[2-[[[4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]carbonyl]amino]ethyl]methanesulfonamide
417726-91-1P, N-[5-Chloro-2-[2-[8-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]phenyl]methanesulfonamide
417726-92-2P, N-[5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]pyridin-3-yl]methanesulfonamide
417726-93-3P, N-[6-Methyl-3-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]pyridin-2-yl]methanesulfonamide
417728-09-7P, 5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of bridged piperazine derivs. as inhibitors of chemokines binding to CCR1 receptors)

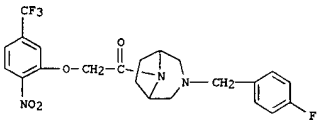
RN 417726-39-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(4-fluorophenyl)methyl]-8-[[2-nitro-4-(trifluoromethyl)phenoxy]acetyl]- (9CI) (CA INDEX NAME)



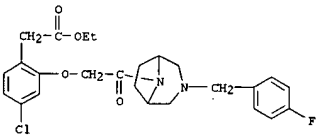
RN 417726-40-0 CAPLUS
CN Benzamide, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



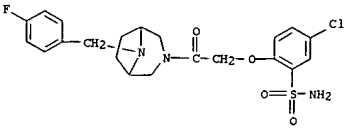
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-45-5 CAPLUS
CN Benzeneacetic acid, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-, ethyl ester (9CI) (CA INDEX NAME)

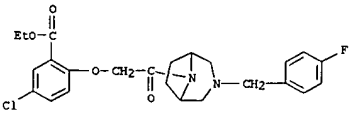


RN 417726-46-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[[2-(aminosulfonyl)-4-chlorophenoxy]acetyl]-8-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

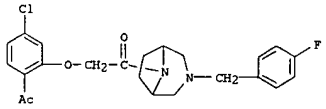


RN 417726-47-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[[2-(aminosulfonyl)-5-chlorophenoxy]acetyl]-8-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

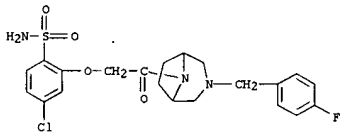
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 417726-41-1 CAPLUS
CN Benzoic acid, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-, ethyl ester (9CI) (CA INDEX NAME)



RN 417726-42-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[(2-acetyl-5-chlorophenoxy)acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

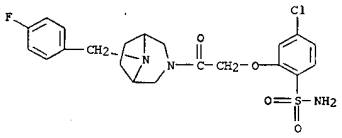


RN 417726-43-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[2-(aminosulfonyl)-5-chlorophenoxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

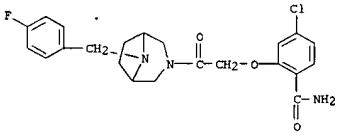


RN 417726-44-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(4-fluorophenyl)methyl]-8-[[2-nitro-5-(trifluoromethyl)phenoxy]acetyl]- (9CI) (CA INDEX NAME)

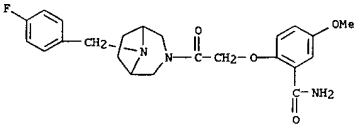
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



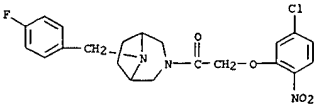
RN 417726-48-8 CAPLUS
CN Benzamide, 4-chloro-2-[2-[8-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



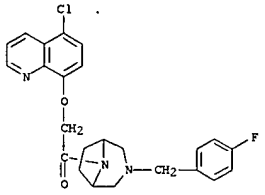
RN 417726-49-9 CAPLUS
CN Benzamide, 2-[2-[8-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]-5-methoxy- (9CI) (CA INDEX NAME)



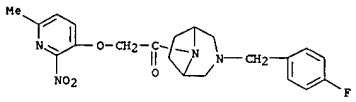
RN 417726-50-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(5-chloro-2-nitrophenoxy)acetyl]-8-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



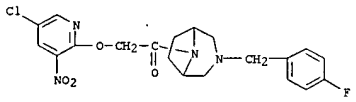
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 417726-51-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[(5-chloro-8-quinolinyl)oxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 417726-52-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(4-fluorophenyl)methyl]-8-[[(6-methyl-2-nitro-3-pyridinyl)oxy]acetyl]- (9CI) (CA INDEX NAME)

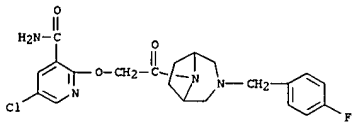


RN 417726-53-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[(5-chloro-3-nitro-2-pyridinyl)oxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

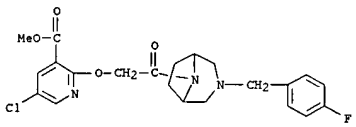


RN 417726-54-6 CAPLUS
CN 3-Pyridinecarboxamide, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

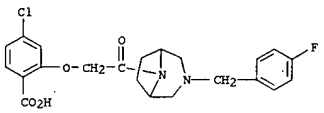
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-55-7 CAPLUS
CN 3-Pyridinecarboxylic acid, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-, methyl ester (9CI) (CA INDEX NAME)

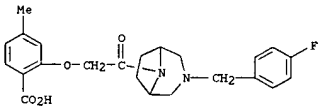


RN 417726-57-9 CAPLUS
CN Benzoic acid, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

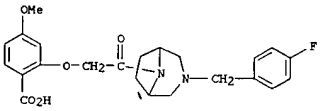


RN 417726-58-0 CAPLUS
CN Benzoic acid, 2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-4-methyl- (9CI) (CA INDEX NAME)

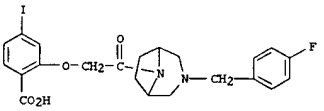
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



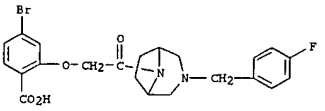
RN 417726-59-1 CAPLUS
CN Benzoic acid, 2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-4-methoxy- (9CI) (CA INDEX NAME)



RN 417726-60-4 CAPLUS
CN Benzoic acid, 2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-4-iodo- (9CI) (CA INDEX NAME)

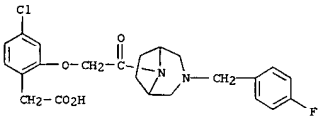


RN 417726-61-5 CAPLUS
CN Benzoic acid, 4-bromo-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

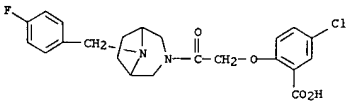


RN 417726-62-6 CAPLUS
CN Benzeneacetic acid, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

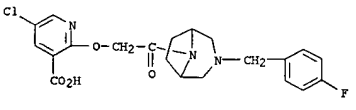
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



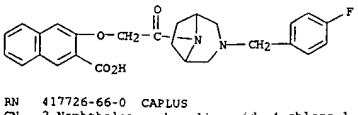
RN 417726-63-7 CAPLUS
CN Benzoic acid, 5-chloro-2-[2-[8-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



RN 417726-64-8 CAPLUS
CN 3-Pyridinecarboxylic acid, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

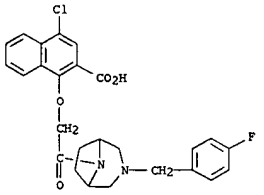


RN 417726-65-9 CAPLUS
CN 2-Naphthalenecarboxylic acid, 3-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

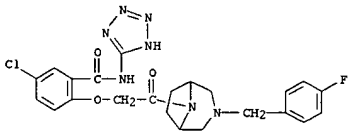


RN 417726-66-0 CAPLUS
CN 2-Naphthalenecarboxylic acid, 4-chloro-1-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

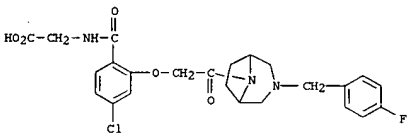
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-67-1 CAPLUS
CN Benzamide, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-1H-tetrazol-5-yl- (9CI) (CA INDEX NAME)

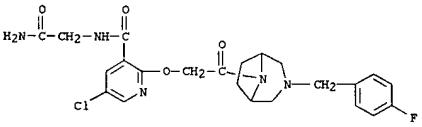


RN 417726-68-2 CAPLUS
CN Glycine, N-[4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoyl]- (9CI) (CA INDEX NAME)

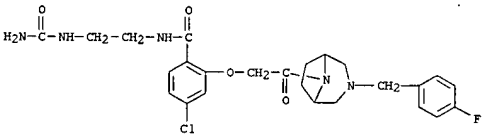


RN 417726-69-3 CAPLUS
CN Benzamide, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-(methylsulfonyl)- (9CI) (CA INDEX NAME)

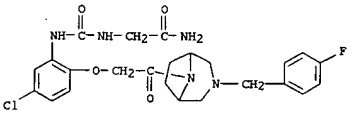
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-73-9 CAPLUS
CN Benzamide, N-[2-[(aminocarbonyl)amino]ethyl]-4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

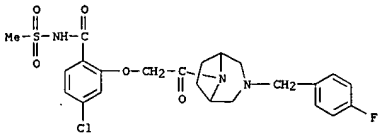


RN 417726-74-0 CAPLUS
CN Acetamide, 2-[[[[5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

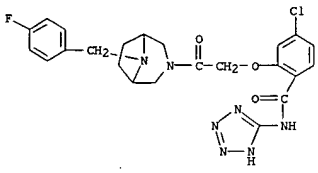


RN 417726-75-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[2-[(aminocarbonyl)amino]-5-chlorophenoxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

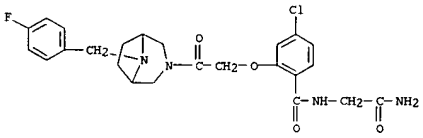
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-70-6 CAPLUS
CN Benzamide, 4-chloro-2-[2-[8-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]-N-1H-tetrazol-5-yl- (9CI) (CA INDEX NAME)

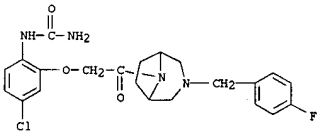


RN 417726-71-7 CAPLUS
CN Benzamide, N-(2-amino-2-oxoethyl)-4-chloro-2-[2-[8-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

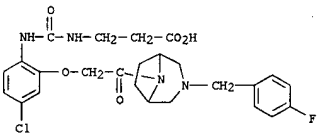


RN 417726-72-8 CAPLUS
CN 3-Pyridinecarboxamide, N-(2-amino-2-oxoethyl)-5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)

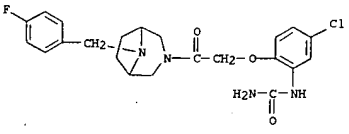
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-76-2 CAPLUS
CN .beta.-Alanine, N-[[[4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]phenyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

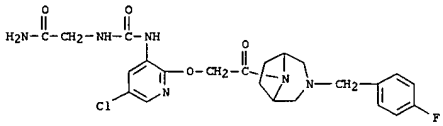


RN 417726-77-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[[2-[(aminocarbonyl)amino]-4-chlorophenoxy]acetyl]-8-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

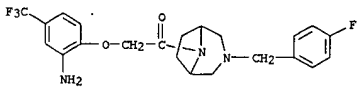


RN 417726-78-4 CAPLUS
CN Acetamide, 2-[[[[5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-3-pyridinyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

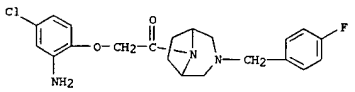
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



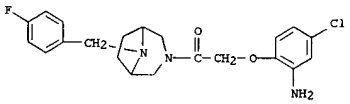
RN 417726-80-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[2-amino-4-(trifluoromethyl)phenoxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



RN 417726-81-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[(2-amino-4-chlorophenoxy)acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

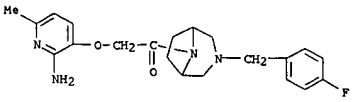


RN 417726-82-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(2-amino-4-chlorophenoxy)acetyl]-8-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

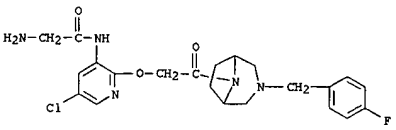


RN 417726-84-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[(2-amino-6-methyl-3-pyridinyl)oxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

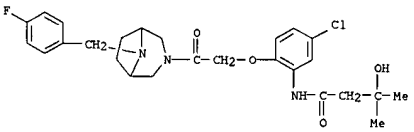
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-85-3 CAPLUS
CN Acetamide, 2-amino-N-[5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-3-pyridinyl]- (9CI) (CA INDEX NAME)

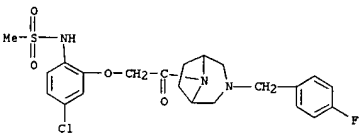


RN 417726-86-4 CAPLUS
CN Butanamide, N-[5-chloro-2-[2-[8-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]-2-oxoethoxy]phenyl]-3-hydroxy-3-methyl- (9CI) (CA INDEX NAME)

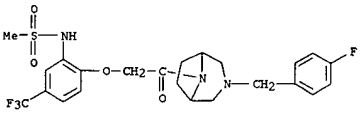


RN 417726-87-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[5-chloro-2-[(methylsulfonyl)amino]phenoxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

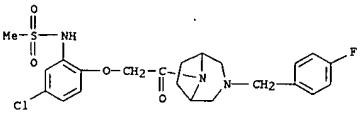
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-88-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(4-fluorophenyl)methyl]-8-[[2-[(methylsulfonyl)amino]-4-(trifluoromethyl)phenoxy]acetyl]- (9CI) (CA INDEX NAME)

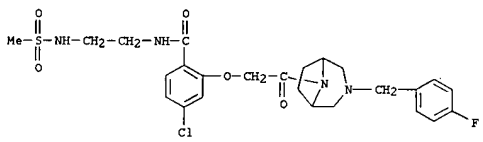


RN 417726-89-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[4-chloro-2-[(methylsulfonyl)amino]phenoxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

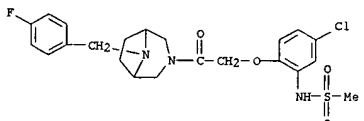


RN 417726-90-0 CAPLUS
CN Benzamide, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-N-[2-[(methylsulfonyl)amino]ethyl]- (9CI) (CA INDEX NAME)

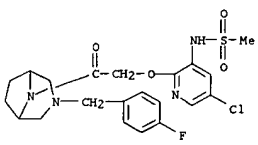
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417726-91-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[[4-chloro-2-[(methylsulfonyl)amino]phenoxy]acetyl]-8-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

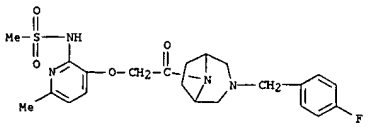


RN 417726-92-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[[[5-chloro-3-[(methylsulfonyl)amino]-2-pyridinyl]oxy]acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)

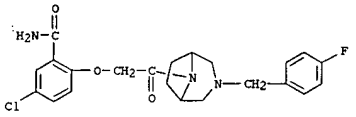


RN 417726-93-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-[(4-fluorophenyl)methyl]-8-[[[6-methyl-2-[(methylsulfonyl)amino]-3-pyridinyl]oxy]acetyl]- (9CI) (CA INDEX NAME)

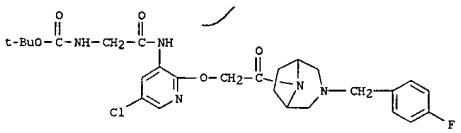
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 417728-09-7 CAPLUS
CN Benzamide, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



IT **417727-51-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of bridged piperazine derivs. as inhibitors of chemokines binding to CCR1 receptors)
RN 417727-51-6 CAPLUS
CN Carbamic acid, [2-[[5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-3-pyridinyl]amino]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

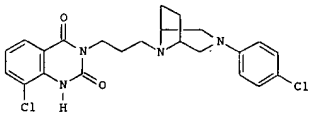


IT **417727-48-1**, 4-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid methyl ester
417727-49-2, 5-Chloro-2-[2-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]benzoic acid **417727-50-5**
, 2-(5-Chloro-2-nitrophenoxy)-1-[3-(4-fluorobenzyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethanone

L17 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:104660 CAPLUS
DOCUMENT NUMBER: 136:151174
TITLE: Preparation of 3-[(arylazabicycloalkyl)alkyl]quinazoline-2,4-diones as serotonin reuptake inhibitors and 5-HT2A receptor antagonists
INVENTOR(S): Butler, Todd William; Fliri, Anton Franz Josef; Gallaschun, Randall James
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 68 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1178048	A1	20020206	EP 2001-306629	20010802
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002052355	A1	20020502	US 2001-920500	20010801
US 6552015	B2	20030422		
BR 2001003210	A	20020326	BR 2001-3210	20010803
JP 2002114789	A2	20020416	JP 2001-236982	20010803

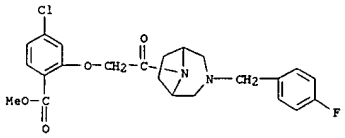
PRIORITY APPLN. INFO.: US 2000-222707P P 20000803
OTHER SOURCE(S): MARPAT 136:151174
GI



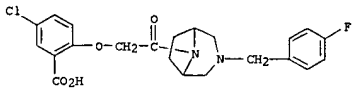
II

AB R(CH2)nZR1 [I; e.g., (un)substituted 2,4-dioxoquinazolin-3-yl; R1 = e.g., (un)substituted Ph; Z = azabicycloalkylene; n = 3 or 4] were prepd. Thus, 3,2-Cl(H2N)C6H3CO2H underwent cyclocondensation/cyclization with Cl(CH2)3NCO to give 8-chloro-3,4-dihydro-2H-1-oxa-4a,9-diazaanthracene-10-one which underwent aminative ring opening with 3-(4-chlorophenyl)-3,8-diazabicyclo[3.2.1]octane to give title compd. II. Data for biol. activity of I were given.
IT **395059-29-7P 395059-55-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 3-[(arylazabicycloalkyl)alkyl]quinazoline-2,4-diones as serotonin reuptake inhibitors and 5-HT2A receptor antagonists)
RN 395059-29-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(4-fluorophenyl)-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

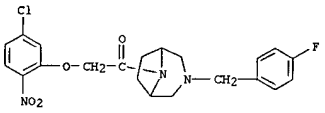
L17 ANSWER 3 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; prepn. of bridged piperazine derivs. as inhibitors of chemokines binding to CCR1 receptors)
RN 417727-48-1 CAPLUS
CN Benzoic acid, 4-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]-, methyl ester (9CI) (CA INDEX NAME)



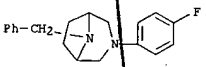
RN 417727-49-2 CAPLUS
CN Benzoic acid, 5-chloro-2-[2-[3-[(4-fluorophenyl)methyl]-3,8-diazabicyclo[3.2.1]oct-8-yl]-2-oxoethoxy]- (9CI) (CA INDEX NAME)



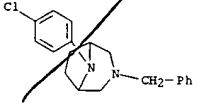
RN 417727-50-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[(5-chloro-2-nitrophenoxy)acetyl]-3-[(4-fluorophenyl)methyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 395059-55-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(4-chlorophenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

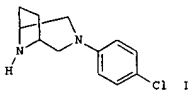


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:104659 CAPLUS
DOCUMENT NUMBER: 136:151188
TITLE: Preparation of 3-phenyl-3,8-diazabicyclo[3.2.1]octanes and analogs as serotonin reuptake inhibitors
INVENTOR(S): Fliri, Anton Franz Josef; Gallaschun, Randall James
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1178047	A1	20020206	EP 2001-306313	20010723
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2001003180	A	20020326	BR 2001-3180	20010801
US 2002068748	A1	20020606	US 2001-920587	20010801
US 6531468	B2	20030311		
JP 2002088084	A2	20020327	JP 2001-235227	20010802

PRIORITY APPLN. INFO.: US 2000-222706P P 20000803
OTHER SOURCE(S): CASREACT 136:151188; MARPAT 136:151188
GI



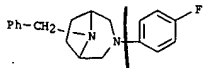
I

AB R3ZR1 [R1 = (un)substituted Ph; R3 = H, alkyl, (hetero)aryl, etc.; Z = e.g., 3,8-diazabicyclo[3.2.1]octane-8,3-diyl] were prepd. as serotonin reuptake inhibitors (no data). Thus, 1-benzyl-2,5-bis(chloromethyl)pyrrolidine (prepn. given) was cyclocondensed with 4-ClC6H4NH2 and the product hydrogenolized to give title compd. I.

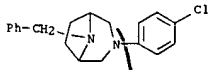
IT **395059-29-7P**, 8-Benzyl-3-(4-fluorophenyl)-3,8-diazabicyclo[3.2.1]octane **395059-41-3P**, 8-Benzyl-3-(4-chlorophenyl)-3,8-diazabicyclo[3.2.1]octane **395059-55-9P**, 3-Benzyl-8-(4-chlorophenyl)-3,8-diazabicyclo[3.2.1]octane
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 3-phenyl-3,8-diazabicyclo[3.2.1]octanes and analogs as serotonin reuptake inhibitors)

RN 395059-29-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(4-fluorophenyl)-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

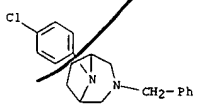
L17 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 395059-41-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(4-chlorophenyl)-8-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 395059-55-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(4-chlorophenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



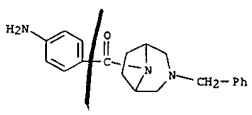
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:629422 CAPLUS
DOCUMENT NUMBER: 136:200161
TITLE: 3,8-Diazabicyclo-[3.2.1]-octane derivatives as analogues of ambasilide, a Class III antiarrhythmic agent
AUTHOR(S): Villa, S.; Barlocco, D.; Cignarella, G.; Papp, G. J.; Balati, B.; Takacs, J.; Varro, A.; Borosy, A.; Keseru, K.; Matyus, P.
CORPORATE SOURCE: Istituto di Chimica Farmaceutica, Universita di Milano, Milan, 20131, Italy
SOURCE: European Journal of Medicinal Chemistry (2001), 36(6), 495-506
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

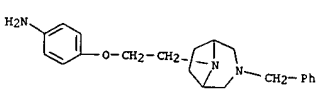
AB Ambasilide, a representative of Class III antiarrhythmics, was reported to prolong the cardiac action potential duration in the dog, with little or no effect on Ca and Na currents. A series of ambasilide analogs have been prepd. possessing the 3,8-diazabicyclo-[3.2.1]-octane moiety instead of the 3,7-diazabicyclo-[3.3.1]-nonane present in ambasilide. The compds. were tested by both in vitro extracellular electrophysiol. assays and by the conventional microelectrode technique. Most compds. tested lengthened the effective refractory period (ERP) with no change or only a slight increase on the impulse conduction time (ICT). Similarly some of the tested compds. lengthened the action potential duration (APD), a typical Class III feature, without exerting any significant effect on the maximal rate of depolarization, therefore apparently lacking Class I antiarrhythmic activity.

IT **401514-09-8P 401514-13-4P**
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and conformation energy anal. of antiarrhythmic diazabicyclooctanes as analogs of ambasilide)

RN 401514-09-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(4-aminobenzoyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



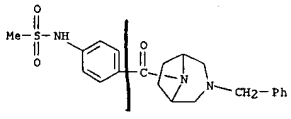
RN 401514-13-4 CAPLUS
CN Benzenamine, 4-[2-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethoxy]- (9CI) (CA INDEX NAME)



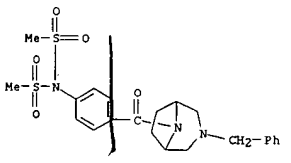
L17 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

IT **401514-10-1P 401514-11-2P 401514-12-3P 401514-14-5P 401514-15-6P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and conformation energy anal. of antiarrhythmic diazabicyclooctanes as analogs of ambasilide)

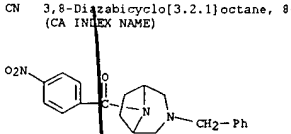
RN 401514-10-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[4-[(methylsulfonyl)amino]benzoyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 401514-11-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-[4-[bis(methylsulfonyl)amino]benzoyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

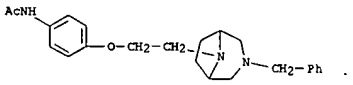


RN 401514-12-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(4-nitrobenzoyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

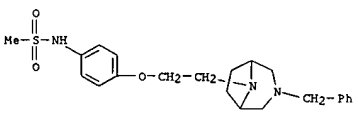


RN 401514-14-5 CAPLUS
CN Acetamide, N-[4-[2-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethoxy]phenyl]- (9CI) (CA INDEX NAME)

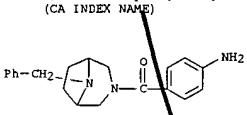
L17 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 401514-15-6 CAPLUS
CN Methanesulfonamide, N-[4-[2-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]ethoxy]phenyl]- (9CI) (CA INDEX NAME)



IT **401514-18-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of antiarrhythmic diazabicyclooctanes via alkylation or amidation of N-protected diazabicyclooctane)
RN 401514-18-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(4-aminobenzoyl)-8-(phenylmethyl)- (9CI) (CA INDEX NAME)



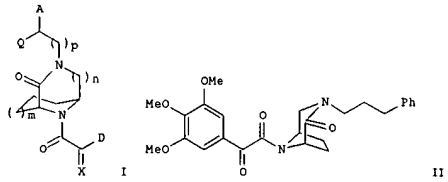
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:435076 CAPLUS
DOCUMENT NUMBER: 135:46205
TITLE: Preparation of neurotrophic bicyclic diamides with peptidylprolyl isomerase (PPIase or rotamase) inhibitory activity
INVENTOR(S): Dubowchik, Gene Michael; Provencal, David Paul
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042245	A1	20010614	WO 2000-US32395	20001128

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

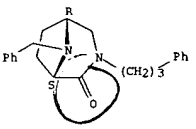
PRIORITY APPLN. INFO.: US 1999-169600P P 19991208
OTHER SOURCE(S): MARPAT 135:46205
GI



AB The invention relates to the design, synthesis, and the peptidylprolyl isomerase (PPIase or rotamase) inhibitory activity of novel bicyclic diamide compds. that are neuroprotective and/or neurotrophic agents (i.e. compds. capable of stimulating growth or proliferation of nervous tissue), and that bind to immunophilins such as FKBP12 and inhibit their rotamase activity. This invention also relates to pharmaceutical compns. comprising these compds. The compds. are encompassed by structure I [X = O, F2; n = 1, 2; m = 0, 1, 2; p = 0, 1; D = alk(en)yl, cycloalk(en),

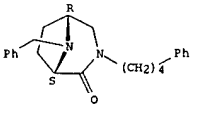
L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
alk(en)yloxy, 2- or 3-indolyl, Ar, Ar-alk(en)yl; Ar = selected (un)substituted carbo- or heterocyclic arom. groups; Q, A = H, Ar, alk(en/yn)yl, cycloalk(en)ylalk(en/yn)yl, their N/O/S-heteroat. analogs, etc.; and their pharmaceutically acceptable salts]. Over 40 examples were prepd. and tested. For instance, (1S,5R)-8-benzyl-3,8-diaza-3-(3-phenylpropyl)bicyclo[3.2.1]octan-2-one (prepn. given) underwent hydrogenolytic debenzylation and amidation with 3,4,5-trimethoxyphenyl-2-oxoacetyl chloride to give title compd. II. In a fluorescence polarization assay of FKBP12 binding, II gave 34% inhibition at 1 .mu.M, and its 3-(3-pyridyloxy)propyl analog gave 98% inhibition.
IT **344462-40-4P 344462-41-5P 344462-42-6P**
344462-43-7P 344462-44-8P 344462-45-9P
344462-47-1P 344462-48-2P 344462-49-3P
344462-50-6P 344462-51-7P 344462-52-8P
344462-53-9P 344462-55-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective prepn. and biol. activity of bicyclic diamides as neuroprotective agents and peptidylprolyl isomerase (PPIase or rotamase) inhibitors)
RN 344462-40-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(phenylmethyl)-3-(3-phenylpropyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 344462-41-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-(4-phenylbutyl)-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

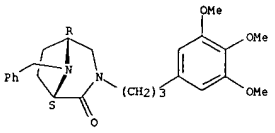
Absolute stereochemistry.



RN 344462-42-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(phenylmethyl)-3-[3-(3,4,5-trimethoxyphenyl)propyl]-, (1S,5R)- (9CI) (CA INDEX NAME)

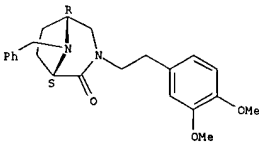
Absolute stereochemistry.

L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



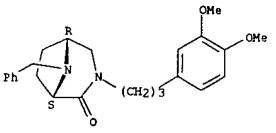
RN 344462-43-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[2-(3,4-dimethoxyphenyl)ethyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 344462-44-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[3-(3,4-dimethoxyphenyl)propyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

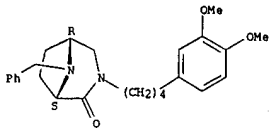
Absolute stereochemistry.



RN 344462-45-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[4-(3,4-dimethoxyphenyl)butyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

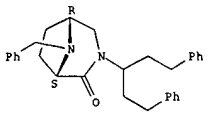
Absolute stereochemistry.

L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



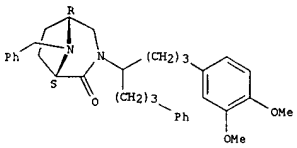
RN 344462-47-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(phenylmethyl)-3-[3-phenyl-1-(2-phenylethyl)propyl]-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 344462-48-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[4-(3,4-dimethoxyphenyl)-1-(3-phenylpropyl)butyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

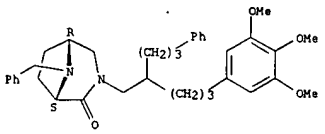
Absolute stereochemistry.



RN 344462-49-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(phenylmethyl)-3-[2-(3-phenylpropyl)-5-(3,4,5-trimethoxyphenyl)pentyl]-, (1S,5R)- (9CI) (CA INDEX NAME)

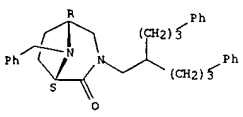
Absolute stereochemistry.

L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



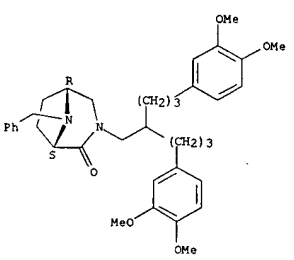
RN 344462-50-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(phenylmethyl)-3-[5-phenyl-2-(3-phenylpropyl)pentyl]-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 344462-51-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[5-(3,4-dimethoxyphenyl)-2-[3-(3,4-dimethoxyphenyl)propyl]pentyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

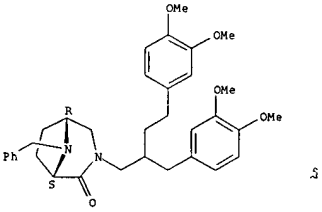
Absolute stereochemistry.



RN 344462-52-8 CAPLUS

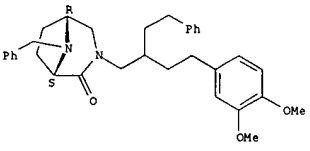
L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[4-(3,4-dimethoxyphenyl)-2-[(3,4-dimethoxyphenyl)methyl]butyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



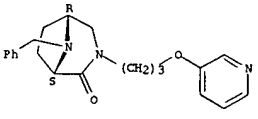
RN 344462-53-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 3-[2-[2-(3,4-dimethoxyphenyl)ethyl]-4-phenylbutyl]-8-(phenylmethyl)-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 344462-55-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(phenylmethyl)-3-[3-(3-pyridinyloxy)propyl]-, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

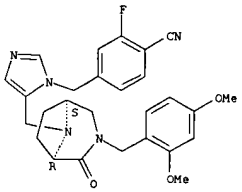
L17 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:122158 CAPLUS
DOCUMENT NUMBER: 134:311179
TITLE: 3,8-Diazabicyclo[3.2.1]octan-2-one Peptide Mimetics: Synthesis of a Conformationally Restricted Inhibitor of Farnesyltransferase
AUTHOR(S): Dinsmore, Christopher J.; Bergman, Jeffrey M.; Bogusky, Michael J.; Culberson, J. Christopher; Hamilton, Kelly A.; Graham, Samuel L.
CORPORATE SOURCE: Departments of Medicinal Chemistry Molecular Systems and Cancer Research, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Organic Letters (2001), 3(6), 865-868
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:311179

AB A new synthesis of the 3,8-diazabicyclo[3.2.1]octan-2-one framework is described. Transannular enolate alkylation of piperazinone derivs. provides a flexible route to highly constrained bicyclic peptidomimetic synthons with substitution at the C.alpha. position. The chem. was used to produce a conformationally constrained farnesyltransferase inhibitor, which aided the elucidation of enzyme-bound conformation.

IT **335160-93-5P 335161-00-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of a conformationally restricted farnesyltransferase inhibitor based on 3,8-diazabicyclo[3.2.1]octanone)

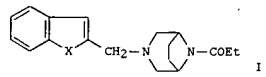
RN 335160-93-5 CAPLUS
CN Benzonitrile, 4-[[5-[[(1R,5S)-3-[(2,4-dimethoxyphenyl)methyl]-2-oxo-3,8-diazabicyclo[3.2.1]oct-8-yl]methyl]-1H-imidazol-1-yl]methyl]-2-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

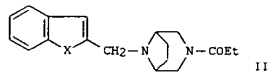


RN 335161-00-7 CAPLUS
CN Benzonitrile, 4-[[5-[[(1R,5S)-3-[(2-chloro-5-[(methylsulfonyl)oxy]phenyl]methyl]-2-oxo-3,8-diazabicyclo[3.2.1]oct-8-yl]methyl]-1H-imidazol-1-yl]methyl]-2-fluoro- (9CI) (CA INDEX NAME)

L17 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:244249 CAPLUS
DOCUMENT NUMBER: 130:311770
TITLE: Benzocondensed derivatives as rigid analogs of the .mu.-opioid agonist 3(8)-cinnamyl-8(3)-propionyl-3,8-diazabicyclo[3.2.1]octanes: synthesis, modeling, and affinity
AUTHOR(S): Cignarella, G.; Barlocco, D.; Vianello, P.; Villa, S.; Pinna, G. A.; Fadda, P.; Fratta, W.; Toma, L.; Gessi, S.
CORPORATE SOURCE: Istituto di Chimica Farmaceutica e Tossicologica, Milan, 20131, Italy
SOURCE: Farmaco (1998), 53(10,11), 667-674
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



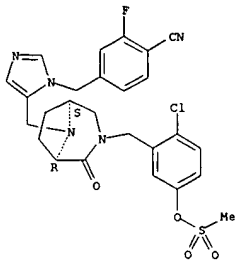
II

AB A new series of rigid analogs I and II [X = O, NH, S, CH:CH, CH2, (CH2)2, (CH2)3] of the previously reported analgesic 3-cinnamyl-8-propionyl-3,8-diazabicyclo[3.2.1]octane and its reverted isomer 3-propionyl-8-cinnamyl(III) were synthesized, in which the cinnamyl substituent is incorporated in benzocondensed bicyclic systems. Binding assays for the affinity towards .mu. receptors indicated that, while in the reverted series II the .beta.-naphthylmethyl and the benzocycloheptenylmethyl deriv. favorably compared with III , all compds. I displayed a .mu.-affinity lower than that of the parent. Modeling studies suggest that the flexibility of the cinnamyl side chain plays an important role for activity.

IT **172207-91-9P 223593-83-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and .mu.-opioid agonist activity of cinnamylpropionyldiazabicyclooctanes)

RN 172207-91-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(1H-indol-2-ylcarbonyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

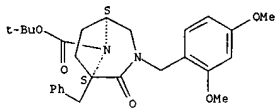
L17 ANSWER 8 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
Absolute stereochemistry.



IT **335160-83-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a conformationally restricted farnesyltransferase inhibitor based on 3,8-diazabicyclo[3.2.1]octanone)

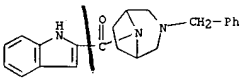
RN 335160-83-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-[(2,4-dimethoxyphenyl)methyl]-2-oxo-1-(phenylmethyl)-, 1,1-dimethylethyl ester, (1S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

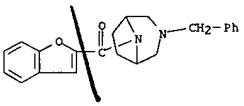


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 223593-83-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(2-benzofuranylcarbonyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



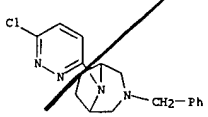
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:88086 CAPLUS
DOCUMENT NUMBER: 128:97657
TITLE: Mono- and Disubstituted-3,8-diazabicyclo[3.2.1]octane Derivatives as Analgesics Structurally Related to Epibatidine: Synthesis, Activity, and Modeling
AUTHOR(S): Barlocco, Daniela; Cignarella, Giorgio; Tondi, Donatella; Vianello, Paola; Villa, Stefania; Bartolini, Alessandro; Ghelardini, Carla; Galeotti, Nicoletta; Anderson, David J.; Kuntzweiler, Theresa A.; Colombo, Diego; Toma, Lucio
CORPORATE SOURCE: Istituo di Chimica Farmaceutica e Tossio, Universita Degli Studi di Milano, Milan, 20131, Italy
SOURCE: Journal of Medicinal Chemistry (1998), 41(5), 674-681
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of 3,8-diazabicyclo[3.2.1]octanes substituted either at the 3 position or at the 8 position by a chlorinated heteroaryl ring were synthesized, as potential analogs of the potent natural analgesic epibatidine. When tested in the hot plate assay, the majority of the compds. showed significant effects, the most interesting being the 3-(6-chloro-3-pyridazinyl)-3,8-diazabicyclo[3.2.1]octane (I). At a s.c. dose of 1 mg/kg, I induced a significant increase in the pain threshold, its action lasting for about 45 min. 1A also demonstrated good protection at a dose of 5 mg/kg in the mouse abdominal constriction test, while at 20 mg/kg it completely prevented the constrictions in the animals. Administration of naloxone (1 mg/kg i.p.) did not antagonize its antinociception while mecamylamine (2 mg/kg i.p.) did, thus suggesting the involvement of the nicotinic system in its action. Binding studies confirmed high affinity for the .alpha.4.beta.2 nAChR subtype (Ki = 4.1 .+-. 0.21 nM). NAChR functional activity studies on three different cell lines showed that I was devoid of any activity at the neuromuscular junction. Finally, due to the analogy in their pharmacol. profile with that of epibatidine, compds. were compared from a structural and conformational point of view through theor. calcns. and high-field 1H NMR spectroscopy. Results indicate that all of them present one conformation similar to that of epibatidine.

IT **201162-43-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, activity, and modeling of mono- and disubstituted-3,8-diazabicyclo[3.2.1]octane derivs. as analgesics structurally related to epibatidine)
RN 201162-43-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(6-chloro-3-pyridazinyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

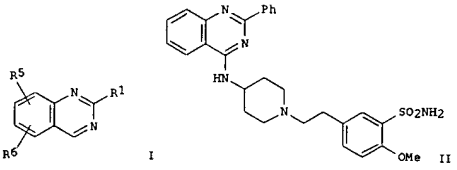
L17 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L17 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:567069 CAPLUS
DOCUMENT NUMBER: 125:221856
TITLE: Preparation of quinazoline derivatives as adrenergic .alpha.1C receptor antagonists
INVENTOR(S): Andrews, Robert Carl; Brown, Peter Jonathan; Deaton, David Norman; Drewry, David Harold; Foley, Michael Andrew; Garrison, Deanna T.; Marron, Brian Edward; Smalley, Terrence L.; Berman, Judd M.; Noble, Stewart Alywyn
PATENT ASSIGNEE(S): Glaxo Inc, USA
SOURCE: Brit. UK Pat. Appl., 190 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2295387	A1	19960529	GB 1994-23635	19941123

PRIORITY APPLN. INFO.: GB 1994-23635 19941123
OTHER SOURCE(S): MARPAT 125:221856
GI

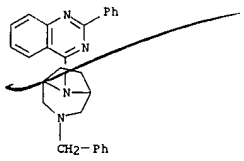


I II

AB Title compds. [I; R = Z1Z2 = R4; R1 = H, halo, alkyl, alkoxy, etc.; R4 = H, (di)(alkyl)amino, phenyl(oxy), etc.; R5,R6 = H, OH, halo, alkyl, alkoxy; Z1 = NH, 2-(piperazine-1,4-diyl)ethylimino, iminopyridine-5,2-diylimino, etc.; Z2 = bond, (un)substituted alkylene] were prepd. as adrenergic .alpha.1C receptor antagonists (no data). Thus, 4-chloro-2-phenylquinazoline was aminated by 4-amino-1-benzylpiperidine and the deprotected product N-alkylated by 5-(2-chloroethyl)-2-methoxybenzenesulfonamide (prepn. given) to give title compd. II.

IT **181115-69-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinazoline derivs. as adrenergic .alpha.1C receptor antagonists)
RN 181115-69-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(phenylmethyl)-8-(2-phenyl-4-quinazolinyl)- (9CI) (CA INDEX NAME)

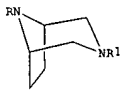
L17 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L17 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:994354 CAPLUS
DOCUMENT NUMBER: 124:55984
TITLE: 3,8-Diazabicyclo[3.2.1]octane derivatives having analgesic activity
INVENTOR(S): Cignarella, Giorgio
PATENT ASSIGNEE(S): Riace Establishment, Liechtenstein
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9523152	A1	19950831	WO 1995-EP476	19950210
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MX, NL, NO, NZ, PL, PT, RO, RU, SE, SI, SK, TJ, TT, UA, UG, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9518085	A1	19950911	AU 1995-18085	19950210
EP 746560	A1	19961211	EP 1995-909700	19950210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5672601	A	19970930	US 1996-696948	19960822

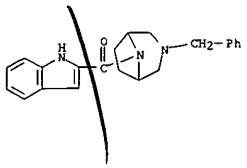
PRIORITY APPLN. INFO.: IT 1994-MI326 19940223
WO 1995-EP476 19950210
OTHER SOURCE(S): CASREACT 124:55984; MARPAT 124:55984
GI



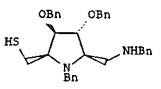
I

AB Title compds. I and their pharmaceutically acceptable salts are claimed and/or prepd. [wherein R .noteq. R1; R, R1 = straight or branched C2-8 acyl, CH2AB; A = bond between 2 C atoms, CH:CH, or CH2CO; B = C6-10 aryl, (un)substituted with .gtoreq. 1 of CONHR, carboxy, cyano, NO2, or NHCOR; or (un)substituted arom. heterocyclic or alicyclic group with 5 or 6 members in the ring, optionally benzocondensed, contg. .gtoreq. 1 of N, O, or S; when R or R1 = propionyl, the other .noteq. cinnamyl or p-nitrocinnamyl; when R = propionyl, R1 .noteq. o- or m-nitrocinnamyl]. I have central analgesic activity comparable to morphine, and bind selectively to opioid .mu. receptors with similar affinity. However, I are substantially free of withdrawal phenomena, as detd. by the jumping test in mice, where activity was 3-20 times lower than morphine after 21 analgesically equipotent doses in 7 days (nó addnl. data). For example,

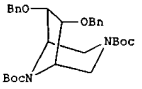
L17 ANSWER 12 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
N-alkylation of N8-acetyl-3,8-diazabicyclo[3.2.1]octane with cinnamyl chloride and K2CO3 in refluxing Me2CO gave I [R = Ac; R1 = CH2CH:CHPh].
IT **172207-91-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of diazabicyclooctane derivs. as analgesics)
RN 172207-91-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(1H-indol-2-ylcarbonyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 13 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:898142 CAPLUS
DOCUMENT NUMBER: 124:117785
TITLE: Concise synthesis of new homoaza sugars. Fully substituted, functionally diverse pyrrolidines
AUTHOR(S): Campanini, Laurence; Dureult, Annie; Depezay, Jean-Claude
CORPORATE SOURCE: Lab. Chim. Biochim. Pharmacologiques Toxicoloqiques, Univ. Rene Descartes, Paris, 75270, Fr.
SOURCE: Tetrahedron Letters (1995), 36(44), 8015-18
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



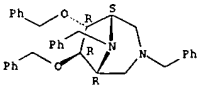
I



II

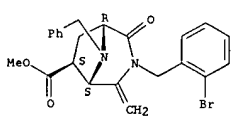
AB Five-membered deoxyaza sugars, e.g. I, of D-gluco configuration, bearing an aminomethyl, a bromomethyl or a thiomethyl group at the pseudo anomeric position, were prepd. by nucleophilic opening of C2 sym. bis-aziridines followed by chemoselective transformations of the nucleophile. The 1-bromo-2,5-imino-D-glucitol could be converted into attractive bicyclic compds., e.g. II.
IT **172795-11-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of pyrrolidine homoaza sugars via nucleophilic ring opening and intramol. cyclocondensation of bis-aziridines)
RN 172795-11-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 6,7-bis(phenylmethoxy)-3,8-bis(phenylmethyl)-, [1R-(6-endo,7-exo)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

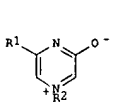


L17 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:502804 CAPLUS
DOCUMENT NUMBER: 123:198662
TITLE: Synthesis of 5,7,8,9,10,11-hexahydro-7-oxo-8,11-iminoazepino[1,2-b]isoquinolines
AUTHOR(S): Peters, David A.; Yates, Nicholas D.; Scopes, David I. C.; Joule, John A.
CORPORATE SOURCE: Chem. Dep., Univ. Manchester, Manchester, M13 9PL, UK
SOURCE: Heterocycles (1995), 40(2), 983-91
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:198662
AB Me 4-methylene-2-oxo-3,8-diazabicyclo[3.2.1]octane-6-exo-6-carboxylates have been converted into Me 5,7,8,9,10,11-hexahydro-7-oxo-8,11-iminoazepino[1,2-b]isoquinoline-10-carboxylates.
IT **167874-03-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of hexahydroiminoazepinoisoquinolines)
RN 167874-03-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 3-[(2-bromophenyl)methyl]-4-methylene-2-oxo-8-(phenylmethyl)-, methyl ester, exo- (9CI) (CA INDEX NAME)

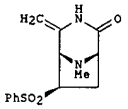
Relative stereochemistry.



L17 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:332276 CAPLUS
DOCUMENT NUMBER: 123:198733
TITLE: 1,3-Dipolar cycloadditions to oxidopyraziniums
AUTHOR(S): Yates, Nicholas D.; Peters, David A.; Allway, Philip A.; Beddoes, Roy L.; Scopes, David I. C.; Joule, John A.
CORPORATE SOURCE: Chem. Dep., Univ. Manchester, Manchester, M13 9PL, UK
SOURCE: Heterocycles (1995), 40(1), 331-47
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



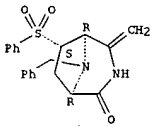
II

AB The cycloaddn. of dipolarophiles to oxidopyraziniums I (R1 = Me, R2 = Me, benzyl; R1 = 3-methoxybenzyl, R2 = Me) are described. Bicyclic products such as II are obtained.

IT **167418-00-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of)

RN 167418-00-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 4-methylene-8-(phenylmethyl)-6-(phenylsulfonyl)-, exo- (9CI) (CA INDEX NAME)

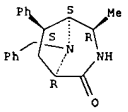
Relative stereochemistry.



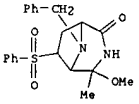
IT **167418-05-5P 167418-06-6P 167418-07-7P**
167418-15-7P 167418-19-1P 167418-22-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 167418-05-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 4-methylene-8-(phenylmethyl)-6-(4-

L17 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

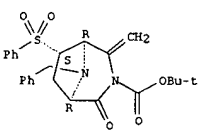


RN 167418-19-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 4-methoxy-4-methyl-8-(phenylmethyl)-6-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



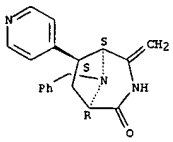
RN 167418-22-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-carboxylic acid, 4-methylene-2-oxo-8-(phenylmethyl)-6-(phenylsulfonyl)-, 1,1-dimethylethyl ester, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



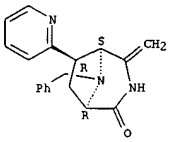
L17 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
pyridinyl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



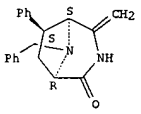
RN 167418-06-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 4-methylene-8-(phenylmethyl)-6-(2-pyridinyl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 167418-07-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 4-methylene-6-phenyl-8-(phenylmethyl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 167418-15-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 4-methyl-6-phenyl-8-(phenylmethyl)-, (endo,endo)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L17 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:77490 CAPLUS
DOCUMENT NUMBER: 120:77490
TITLE: The asymmetric synthesis of (-)-quinocarcin via a 1,3-dipolar cycloadditive strategy
AUTHOR(S): Garner, Philip; Ho, Wen Bin; Shin, Hunwoo
CORPORATE SOURCE: Dep. Chem., Case West. Reserve Univ., Cleveland, OH, 44106-7078, USA
SOURCE: Journal of the American Chemical Society (1993), 115(23), 10742-53
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:77490
GI

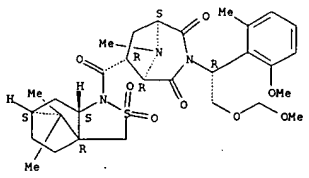
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Details of the asym. synthesis and complete structure elucidation of (-)-quinocarcin (I), an antitumor antibiotic that inhibits DNA (and in some systems RNA) synthesis, are reported. Key steps in the synthesis include the use of an auxiliary-controlled 1,3-dipolar cycloaddn. reaction (II + III .fwdarw. IV) as well as an unprecedented intramol. imide olefination (V .fwdarw. VI) to assemble the 3,8-diazabicyclo[3.2.1]octane (CD ring) and isoquinoline (B ring) subunits of I in a stereo- and regiocontrolled manner. A comparison of the optical rotations of synthetic and natural quinocarcin confirms that the abs. configuration of this antibiotic is as depicted. Conclusive evidence for the (2aR) stereochem. in I is provided by a NOESY expt. on quinocarcin citrate.

IT **139527-59-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and bromination of)

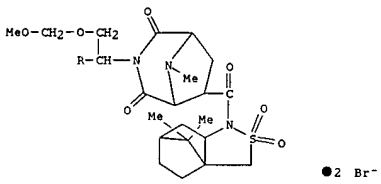
RN 139527-59-6 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-1-[[3-[2-(methoxymethoxy)-1-(2-methoxy-6-methylphenyl)ethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

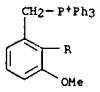


IT **139527-61-0P**

L17 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and intramol. regioselective cyclization of)
RN 139527-61-0 CAPLUS
CN Phosphonium, [[3-methoxy-2-[2-(methoxymethoxy)-1-[8-methyl-2,4-dioxo-6-[(tetrahydro-8,8-dimethyl-2,2-dioxido-3H-3a,6-methano-2,1-benzisothiazol-1(4H)-yl)carbonyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]ethyl]phenyl]methyl]triphenyl-, bromide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)



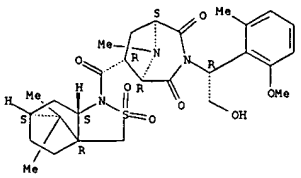
●2 Br⁻



IT **139527-58-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and methoxymethylation of)
RN 139527-58-5 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-1-[[3-[2-hydroxy-1-(2-methoxy-6-methylphenyl)ethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

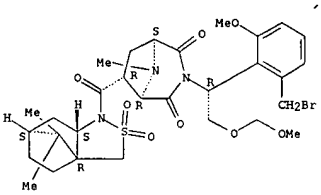
Absolute stereochemistry. Rotation (+).

L17 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

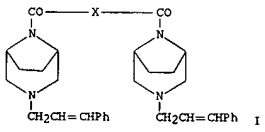


IT **139527-60-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with triphenylphosphine)
RN 139527-60-9 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[1-[2-(bromomethyl)-6-methoxyphenyl]-2-(methoxymethoxy)ethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L17 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:551940 CAPLUS
DOCUMENT NUMBER: 119:151940
TITLE: Synthesis and opioid receptor affinity of bivalent ligands derived from 3,8-diazabicyclo(3.2.1)octanes
AUTHOR(S): Barlocco, Daniela; Fadda, Paola; Fratta, Walter
CORPORATE SOURCE: Ist. Chim. Farm. Toss., Univ. Milano, Milan, 20131, Italy
SOURCE: Farmaco (1993), 48(3), 387-96
CODEN: FRMCE8; ISSN: 0014-827X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

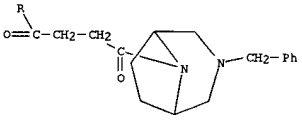


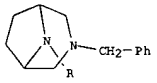
I

AB A new series of bivalent ligands [I, X = (CH2)2, (CH2)3, (CH2)4 or trans CH2-CH=CH-CH2], derived from the previously reported analgesic 3-cinnamyl-8-propionyl-3,8-diazabicyclo(3.2.1)octane (II), has been synthesized and tested in vitro for their affinity towards opioid receptors and in vivo for their analgesic potency. None of the new compds. showed either appreciable affinity for opioid receptors or analgesic activity comparable to that of the model II.

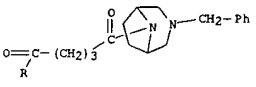
IT **149771-39-1P 149771-40-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
RN 149771-39-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8,8'-(1,4-dioxo-1,4-butanediyl)bis[3-(phenylmethyl)- (9CI) (CA INDEX NAME)

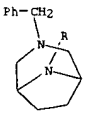
L17 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)





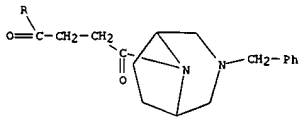
RN 149771-40-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8,8'-(1,5-dioxo-1,5-pentanediyl)bis[3-(phenylmethyl)- (9CI) (CA INDEX NAME)

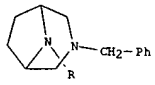




IT **149750-00-5P 150146-11-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and opioid receptor affinity of, analgesic activity in relation to)
RN 149750-00-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8,8'-(1,4-dioxo-1,4-butanediyl)bis[3-(phenylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

L17 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



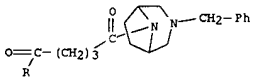


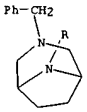
●2 HCl

RN 150146-11-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8,8'-(1,5-dioxo-1,5-pentanediyl)bis[3-(phenylmethyl)-, bis(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

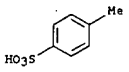
CRN 149771-40-4
CMF C31 H40 N4 O2



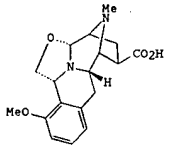


CM 2

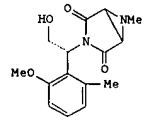
L17 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CRN 104-15-4
CMF C7 H8 O3 S



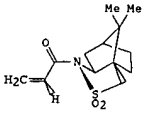
L17 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:173839 CAPLUS
DOCUMENT NUMBER: 116:173839
TITLE: Asymmetric synthesis of (-)-quinocarcin
AUTHOR(S): Garner, Philip; Ho, Wen Bin; Shin, Hunwoo
CORPORATE SOURCE: Dep. Chem., Case West. Reserve Univ., Cleveland, OH, 44106-7078, USA
SOURCE: Journal of the American Chemical Society (1992), 114(7), 2767-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



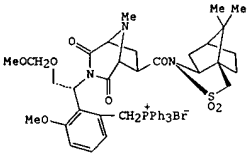
I



II



III



IV

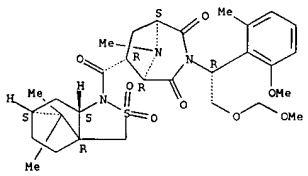
AB The first asym. synthesis of (-)-quinocarcin (I) an antitumor antibiotic isolated from Streptomyces melanovinaceus that inhibits DNA (and in some systems RNA) synthesis, is reported. Key steps in the synthesis include an auxiliary-controlled 1,3-dipolar cycloaddn. reaction between imide II and acrylamide III and an unprecedented intramol. olefination of the imide IV to construct the 3,8-diazabicyclo[3.2.1]octane (CD ring) and isoquinoline (B-ring) subunits of I in a stereo- and regiocontrolled manner. A comparison of the optical rotations of synthetic and natural I confirms that the abs. configuration of this substance is as depicted.

IT **139527-59-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and bromination of)

RN 139527-59-6 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-1-[[3-[2-(methoxymethoxy)-1-(2-methoxy-6-methylphenyl)ethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

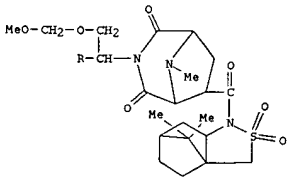
L17 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).

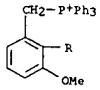


IT **139527-61-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 139527-61-0 CAPLUS
CN Phosphonium, [[3-methoxy-2-[2-(methoxymethoxy)-1-[8-methyl-2,4-dioxo-6-[(tetrahydro-8,8-dimethyl-2,2-dioxido-3H-3a,6-methano-2,1-benzisothiazol-1(4H)-yl)carbonyl]-3,8-diazabicyclo[3.2.1]oct-3-yl]ethyl]phenyl]methyl]triphenyl-, bromide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)



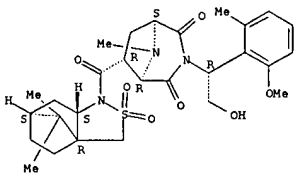
●2 Br⁻



IT **139527-58-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

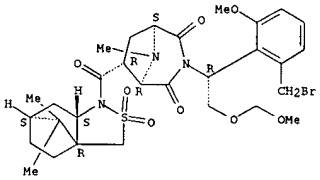
L17 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(prepn. and etherification of)
RN 139527-58-5 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-1-[[3-[2-hydroxy-1-(2-methoxy-6-methylphenyl)ethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

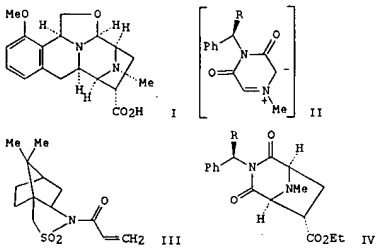


IT **139527-60-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with triphenylphosphine)
RN 139527-60-9 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[1-[2-(bromomethyl)-6-methoxyphenyl]-2-(methoxymethoxy)ethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

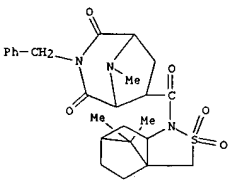


L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:559499 CAPLUS
DOCUMENT NUMBER: 115:159499
TITLE: Development of an asymmetric approach to the 3,8-diazabicyclo[3.2.1]octane moiety of quinocarcin via intramolecular 1,3-dipolar cycloadditions of photochemically generated azomethine ylides
AUTHOR(S): Garner, Philip; Ho, Wen Bin; Grandhee, Sunitha K.; Youngs, Wiley J.; Kennedy, Vance O.
CORPORATE SOURCE: Dep. Chem., Case West. Reserve Univ., Cleveland, OH, 44106-7078, USA
SOURCE: Journal of Organic Chemistry (1991), 56(20), 5893-903
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:159499
GI

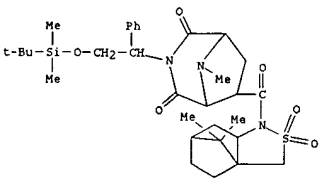


AB Exploratory work culminating in an enantioselective approach to the DNA-reactive alkaloid quinocarcin (I) is detailed. The key step involves auxiliary-controlled dipolar cycloaddn. between photochem. generated azomethine ylides such as II (R = H, CH2OSiMe2CMe3) and Oppolzer's chiral acryloyl sultam (III) to assemble the 6-exo-substituted 3,8-diazabicyclo[3.2.1]octane core of I. The expected re-face selectivity of III was confirmed in one case by x-ray crystallog. anal. of endo-adduct. Removal (and recovery) of the chiral sultam auxiliary can be affected by titanium(IV)-mediated alcoholysis to give ester derivs. of the cycloadducts IV.
IT **127381-61-7P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and crystal structure of)
RN 127381-61-7 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-8,8-dimethyl-1-[[8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-, 2,2-dioxide, [3aS-[1(1R*,5R*,6R*),3a.alpha.,6.alpha.,7a.beta.]]- (9CI)

L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(CA INDEX NAME)

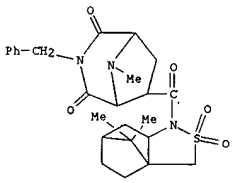


IT **127381-65-1P 127470-56-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and ethanolysis of)
RN 127381-65-1 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aS-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

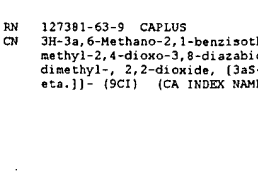


RN 127470-56-8 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-8,8-dimethyl-1-[[8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-, 2,2-dioxide, [3aS-[1(1S*,5R*,6R*),3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

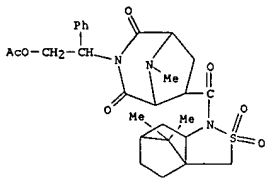


IT **127381-62-8P 127381-63-9P 127381-64-0P**
127420-42-2P 127470-57-9P 135457-93-1P
135481-27-5P 135557-56-1P 135557-57-2P
135558-14-4P 135558-15-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 127381-62-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-acetic acid, 8-methyl-2,4-dioxo-.alpha.-phenyl-6-[(tetrahydro-8,8-dimethyl-2,2-dioxido-3H-3a,6-methano-2,1-benzisothiazol-1(4H)-yl)carbonyl]-, methyl ester, [3aS-[1[1S*,3(S*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

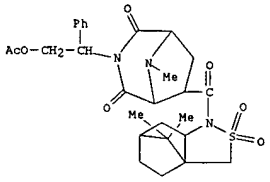


RN 127381-63-9 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-(acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aS-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

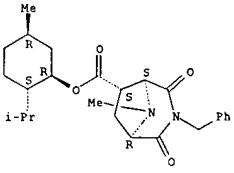


RN 127381-64-0 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-(acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(S*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)



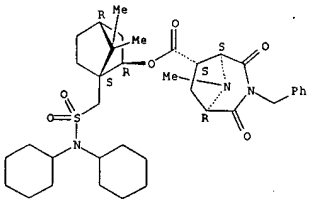
RN 127420-42-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-acetic acid, 8-methyl-2,4-dioxo-.alpha.-phenyl-6-[(tetrahydro-8,8-dimethyl-2,2-dioxido-3H-3a,6-methano-2,1-benzisothiazol-1(4H)-yl)carbonyl]-, methyl ester, [3aS-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



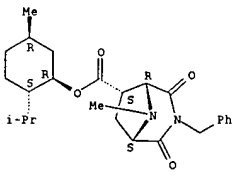
RN 135481-27-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 8-methyl-2,4-dioxo-3-(phenylmethyl)-, 1-[[(dicyclohexylamino)sulfonyl]methyl]-7,7-dimethylbicyclo[2.2.1]hept-2-yl ester, [1R-[1.alpha.,5.alpha.,6.alpha.(1S*,2R*,4R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

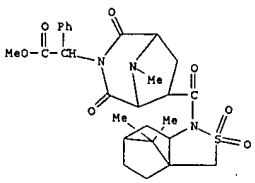


RN 135557-56-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 8-methyl-2,4-dioxo-3-(phenylmethyl)-, 5-methyl-2-(1-methylethyl)cyclohexyl ester, [1S-[1.alpha.,5.alpha.,6.beta.(1S*,2R*,5S*)]]- (9CI) (CA INDEX NAME)

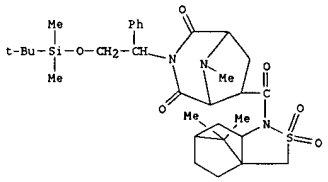
Absolute stereochemistry.



L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 127470-57-9 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(S*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)



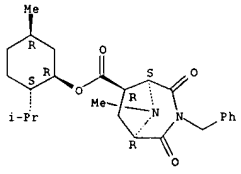
RN 135457-93-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 8-methyl-2,4-dioxo-3-(phenylmethyl)-, 5-methyl-2-(1-methylethyl)cyclohexyl ester, [1R-(1.alpha.,5.alpha.,6.alpha.(1R*,2S*,5R*))]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

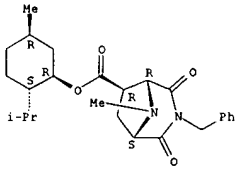
RN 135557-57-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 8-methyl-2,4-dioxo-3-(phenylmethyl)-, 5-methyl-2-(1-methylethyl)cyclohexyl ester, [1R-[1.alpha.,5.alpha.,6.beta.(1R*,2S*,5R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 135558-14-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 8-methyl-2,4-dioxo-3-(phenylmethyl)-, 5-methyl-2-(1-methylethyl)cyclohexyl ester, [1S-[1.alpha.,5.alpha.,6.alpha.(1S*,2R*,5S*)]]- (9CI) (CA INDEX NAME)

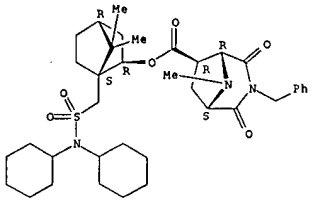
Absolute stereochemistry.



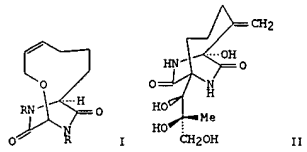
RN 135558-15-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6-carboxylic acid, 8-methyl-2,4-dioxo-3-(phenylmethyl)-, 1-[[(dicyclohexylamino)sulfonyl]methyl]-7,7-dimethylbicyclo[2.2.1]hept-2-yl ester, [1S-[1.alpha.,5.alpha.,6.alpha.(1R*,2S*,4S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

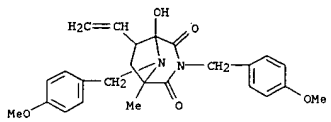
L17 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



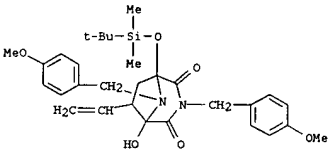
L17 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:536722 CAPLUS
DOCUMENT NUMBER: 115:136722
TITLE: Novel ring contractions via [2,3] Wittig type rearrangements: synthesis of 2-desoxy-2-methylenebicyclomycin
AUTHOR(S): Williams, Robert M.; Sabol, Mark R.; Kim, Hee Doo; Kwast, Andrzej
CORPORATE SOURCE: Dep. Chem., Colorado State Univ., Fort Collins, CO, 80523, USA
SOURCE: Journal of the American Chemical Society (1991), 113(17), 6621-33
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:136722
GI



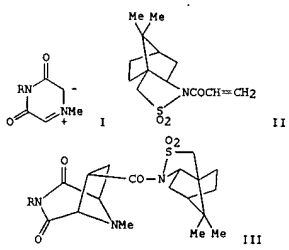
AB Generation of bridgehead carbanions from bicyclo[5.2.2]- and bicyclo[7.2.2]-allyl ether-bridged piperazinediones results in novel ring contractions via unusual [2,3] Wittig and [3,3] Claisen rearrangements. The [2,3] Wittig rearrangement was applied to the oxadiazabicyclotridecanedione I (R = 4-MeOC6H4CH2) in the construction of 2-deoxy-2-methylenebicyclomycin (II).
IT **135365-99-0P 135366-01-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 135365-99-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 6-ethenyl-5-hydroxy-3,8-bis[(4-methoxyphenyl)methyl]-1-methyl- (9CI) (CA INDEX NAME)



L17 ANSWER 20 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 135366-01-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-ethenyl-5-hydroxy-3,8-bis[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

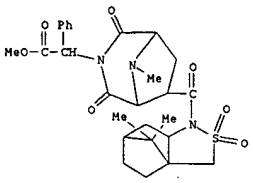


L17 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:424309 CAPLUS
DOCUMENT NUMBER: 113:24309
TITLE: Stereoselective 1,3-dipolar cycloadditions of photochemically generated azomethine ylides to Oppolzer's chiral acryloyl sultam. An asymmetric approach to quinocarcin
AUTHOR(S): Garner, Philip; Ho, Wen Bin
CORPORATE SOURCE: Dep. Chem., Case West. Reserve Univ., Cleveland, OH, 44106-2699, USA
SOURCE: Journal of Organic Chemistry (1990), 55(13), 3973-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

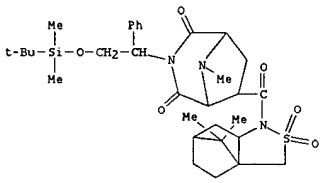


AB Photochem. generated azomethine ylides I [R = PhCH2, PhCH(CO2Me), PhCH(CH2OAc), PhCH(CH2OSiMe2CMe3)] underwent highly selective (ds >25:1) 1,3-dipolar cycloaddns. to the chiral acryloyl sultam (-)-II giving cycloadducts III corresponding to the substituted 3,8-diazabicyclo[3.2.1]octane moiety of quinocarcin with complete stereocontrol. The analogous reaction of with (+)-II provided the diastereomeric adducts, confirming that the stereochem. outcome is under control of the chiral auxiliary. The sultam auxiliary was readily removed (in recoverable form) by Ti(IV) -promoted alcoholysis of the cycloadducts.
IT **127381-62-8P 127381-65-1P 127420-42-2P**
127470-56-8P 127470-57-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alcoholysis of)
RN 127381-62-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-acetic acid, 8-methyl-2,4-dioxo-.alpha.-phenyl-6-[(tetrahydro-8,8-dimethyl-2,2-dioxido-3H-3a,6-methano-2,1-benzisothiazol-1(4H)-yl)carbonyl]-, methyl ester, [3aS-[1[1S*,3(S*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

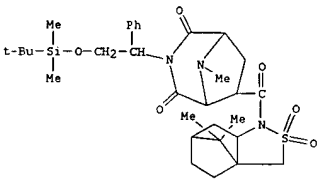


RN 127381-65-1 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aS-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

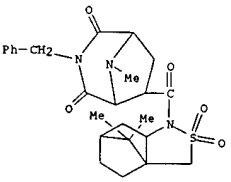


RN 127420-42-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-acetic acid, 8-methyl-2,4-dioxo-.alpha.-phenyl-6-[(tetrahydro-8,8-dimethyl-2,2-dioxido-3H-3a,6-methano-2,1-benzisothiazol-1(4H)-yl)carbonyl]-, methyl ester, [3aS-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

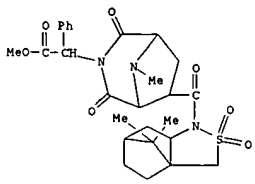


IT **127381-61-7P 127381-63-9P 127381-64-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 127381-61-7 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-8,8-dimethyl-1-[[8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-, 2,2-dioxide, [3aS-[1(1R*,5R*,6R*),3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

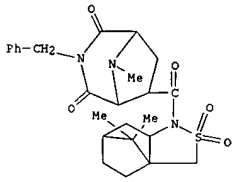


RN 127381-63-9 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-(acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aS-[1[1S*,3(R*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

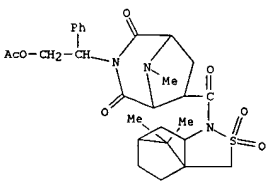


RN 127470-56-8 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, hexahydro-8,8-dimethyl-1-[[8-methyl-2,4-dioxo-3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]-, 2,2-dioxide, [3aS-[1(1S*,5R*,6R*),3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

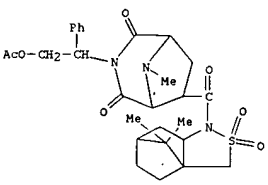


RN 127470-57-9 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(S*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)

L17 ANSWER 21 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 127381-64-0 CAPLUS
CN 3H-3a,6-Methano-2,1-benzisothiazole, 1-[[3-[2-(acetyloxy)-1-phenylethyl]-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]oct-6-yl]carbonyl]hexahydro-8,8-dimethyl-, 2,2-dioxide, [3aR-[1[1S*,3(S*),5R*,6R*],3a.alpha.,6.alpha.,7a.beta.]]- (9CI) (CA INDEX NAME)



L17 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:57646 CAPLUS
DOCUMENT NUMBER: 110:57646
TITLE: Antibacterial naphthyridine- and quinolonecarboxylic acid derivatives
INVENTOR(S): Weber, Abraham; Bouzard, Daniel; Essiz, Munir; Di Cesare, Pierre; Jacquet, Jean Pierre; Remuzon, Phillippe
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8802627	A1	19880421	WO 1987-US2556	19871008
W: AU, DK, FI, HU, JP, KR, NO, RO, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
ZA 8707471	A	19880525	ZA 1987-7471	19871005
DD 266354	A5	19890329	DD 1987-307706	19871006
DD 280530	A5	19900711	DD 1987-327989	19871006
AU 8781581	A1	19880506	AU 1987-81581	19871008
AU 611400	B2	19910613		
EP 288519	A1	19881102	EP 1987-907178	19871008
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 52500	A2	19900728	HU 1986-56	19871008
HU 203753	B	19910930		
DK 8803555	A	19880823	DK 1988-3555	19880628
NO 8803077	A	19880822	NO 1988-3077	19880708
FI 8803894	A	19880823	FI 1988-3894	19880823
CS 270598	B2	19900712	CS 1988-7400	19881110
AU 9176326	A1	19910808	AU 1991-76326	19910501

PRIORITY APPLN. INFO.: US 1986-916752 19861008
CS 1987-7295 19871008
WO 1987-US2556 19871008
OTHER SOURCE(S): MARPAT 110:57646
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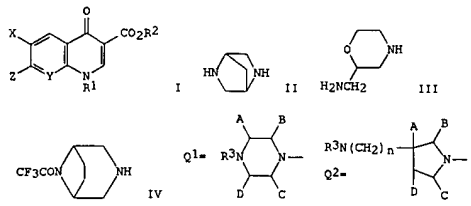
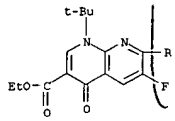
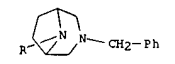


L17 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

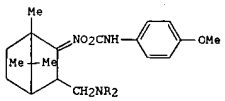
AB The title compds. I [X = F, Cl, Br, CF3, CCl3; Z = Q1, Q2, etc.; A, B, C, D, = H, (substituted) lower alkyl, NH2, OH, F, Cl, etc.; n = 0-3; R1 = CMe3, CMe2CH2Me, CPhMe2, etc.; R2 = H, C1-4 alkyl, alkali and alk. earth metal ions; R3 = H, (substituted) C1-6 alkyl, C3-6 cycloalkyl, etc.; Y = CH, CF, CCl, CBr, N], useful as antibacterials, were prepd., e.g., using amines II, III, IV, etc. Reaction of Et 1-(1,1-dimethylethyl)-1,4-dihydro-6,7,8-trifluoro-4-oxo-3-quinolinecarboxylate with piperazine in MeCN, followed by sapon. and workup, gave 7-piperazinyl-1-(1,1-dimethylethyl)-1,4-dihydro-6,8-difluoro-4-oxo-3-quinolinecarboxylic acid (V). V in vitro exhibited a MIC of 4 .mu.g/mL against Pseudomonas aeruginose. The corresponding MIC of norfloxacin was 0.5 .mu.g/mL.
IT **118329-60-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of naphthyridine and quinolone antibacterials)
RN 118329-60-5 CAPLUS
CN 1,8-Naphthyridine-3-carboxylic acid, 1-(1,1-dimethylethyl)-6-fluoro-1,4-dihydro-4-oxo-7-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]-, ethyl ester (9CI) (CA INDEX NAME)



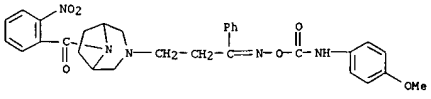


L17 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

L17 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:488088 CAPLUS
DOCUMENT NUMBER: 103:88088
TITLE: Synthesis and pharmacological activity of 3-aminopropiophenones and 3-(aminomethyl)camphors
AUTHOR(S): Occelli, E.; Fontanella, L.; Diena, A.; Schiatti, P.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1985), 40(2), 86-101
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI

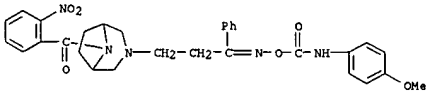


AB Z:CPhCH2CH2NR2.HCl [I, R = alkyl, (substituted) N-contg. heterocyclyl; Z = O, (acyl) hydroxyimino] and the camphor derivs. II (R same as above) were prepd. and their CNS, analgesic, and antiinflammatory activities evaluated.
IT **97669-75-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and CNS activity of)
RN 97669-75-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-propanimine, N-[[[(4-methoxyphenyl)amino]carbonyl]oxy]-8-(2-nitrobenzoyl)-.alpha.-phenyl- (9CI) (CA INDEX NAME)



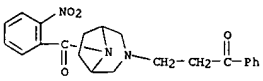
IT **97670-11-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and pharmacol. activities of)
RN 97670-11-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-propanimine, N-[[[(4-methoxyphenyl)amino]carbonyl]oxy]-8-(2-nitrobenzoyl)-.alpha.-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

L17 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

IT **97669-87-9P 97669-99-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 97669-87-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(2-nitrobenzoyl)-3-(3-oxo-3-phenylpropyl)-, monohydrochloride (9CI) (CA INDEX NAME)

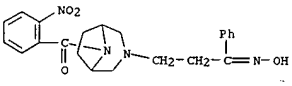


● HCl

RN 97669-99-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-3-propanimine, N-hydroxy-8-(2-nitrobenzoyl)-.alpha.-phenyl-, ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 97669-98-2
CMF C22 H24 N4 O4



CM 2

CRN 144-62-7
CMF C2 H2 O4

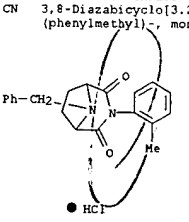
L17 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:423500 CAPLUS
DOCUMENT NUMBER: 101:23500
TITLE: Diazabicyclooctanes with anxiolytic and sedative activity
INVENTOR(S): Pedrazzoli, Andrea; Crisafulli, Emilio
PATENT ASSIGNEE(S): Sanofi, Fr.
SOURCE: Fr. Demande, 14 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2531709	A1	19840217	FR 1982-14127	19820813
FR 2531709	B1	19850111		

PRIORITY APPLN. INFO.: FR 1982-14127 19820813
OTHER SOURCE(S): CASREACT 101:23500
GI

I

AB 3,8-Diazabicyclo[3.2.1]octanes I [one of R and R1 is 2-pyrimidinyl and the other is H, alkyl, Ph, tolyl, PhCH2, 3,4-(CH2O2)C6H3CH2, PhCH:CHCH2, alkanoyl, PhCO, 3,4-(CH2O2)C6H2CO, PhCH:CHCO], which were prepd., are useful as anxiolytics and sedatives (no data). I [R = 3,4-(CH2O2)C6H3CO, R1 = H] was treated with 2-chloropyrimidine and K2CO3 in DMF to give I [R = 3,4-(CH2O2)C6H3CO, R1 = 2-pyrimidinyl].
IT **90478-34-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydride redn. of)
RN 90478-34-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 3-(2-methylphenyl)-8-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

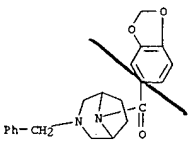


● HCl

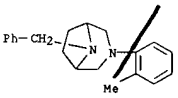
IT **90478-31-2P 90478-35-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

L17 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

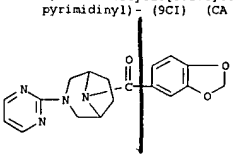
L17 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(prepn. and hydrogenolysis of)
RN 90478-31-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(1,3-benzodioxol-5-ylcarbonyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 90478-35-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(2-methylphenyl)-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

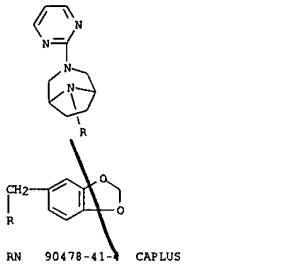


IT **90478-39-0 90478-40-3 90478-41-4 90478-45-8 90478-51-6 90478-52-7 90478-53-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation by, of diazabicyclooctane deriv.)
RN 90478-39-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(1,3-benzodioxol-5-ylcarbonyl)-3-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)

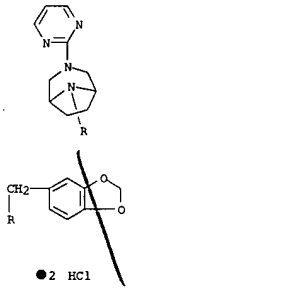


RN 90478-40-3 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(1,3-benzodioxol-5-ylmethyl)-3-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)

L17 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



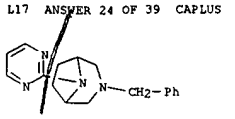
RN 90478-41-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(1,3-benzodioxol-5-ylmethyl)-3-(2-pyrimidinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



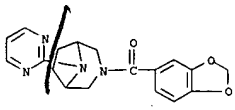
●2 HCl

RN 90478-45-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(phenylmethyl)-8-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)

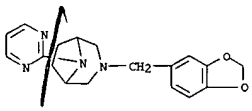
L17 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



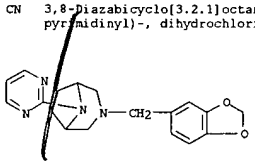
RN 90478-51-6 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(1,3-benzodioxol-5-ylcarbonyl)-8-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)



RN 90478-52-7 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(1,3-benzodioxol-5-ylmethyl)-8-(2-pyrimidinyl)- (9CI) (CA INDEX NAME)

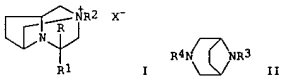


RN 90478-53-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(1,3-benzodioxol-5-ylmethyl)-8-(2-pyrimidinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



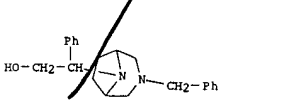
●2 HCl

L17 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1979:72149 CAPLUS
DOCUMENT NUMBER: 90:72149
TITLE: Tricyclic homologs of piperazine. III. Synthesis of 4-substituted hexahydro-1H-2,6-methanopyrolo[1,2-a]pyrazines
AUTHOR(S): Occelli, E.; Fontanella, L.; Testa, E.
CORPORATE SOURCE: Lab. Ric., Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1978), 33(11), 875-84
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI



AB Methanopyrrolopyrazine I (R = H, R1 = R2 = Me, X = Cl) was prepd. by treating II (R3 = H, R4 = CH2Ph) with BrCHMeCO2Et, debenzylating II (R3 = CHMeCO2Et, R4 = CH2Ph), methylating II (R3 = CHMeCO2Et, R4 = H), reducing II (R3 = CHMeCO2Et, R4 = Me), chlorinating the resulting alc., and cyclizing II (R3 = CHMeCH2Cl, R4 = Me) with base. I (R = R1 = Me, R2 = CH2Ph, X = MeSO3; R = H, R1 = Ph, R2 = CH2Ph, X = Cl) were similarly prepd. The latter 2 compds. gave 23 and 6% decrease resp. in gastrocnemic muscle contraction in rabbits at 2 mg/kg i.v.

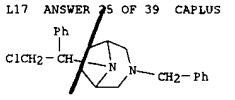
IT **69099-93-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and chlorination of)
RN 69099-93-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-8-ethanol, .beta.-phenyl-3-(phenylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

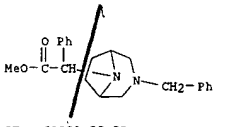
IT **69099-94-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)
RN 69099-94-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-(2-chloro-1-phenylethyl)-3-(phenylmethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

L17 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

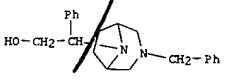


●2 HCl

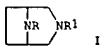
IT **69099-91-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 69099-91-8 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-8-acetic acid, .alpha.-phenyl-3-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



IT **69099-92-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 69099-92-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-8-ethanol, .beta.-phenyl-3-(phenylmethyl)-(9CI) (CA INDEX NAME)

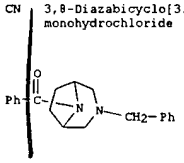


L17 ANSWER 26 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:509371 CAPLUS
DOCUMENT NUMBER: 89:109371
TITLE: Bicyclic piperazine homologs. XIV. Synthesis ad analgesic activity of 3,8-diazabicyclo[3.2.1]octane derivatives
AUTHOR(S): Occelli, E.; Fontanella, L.; Diena, A.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1978), 33(6), 401-20
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI



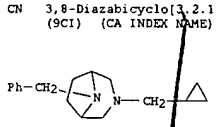
I

AB 2,6-Ethanopiperazines I [R = CH2CH:CMe2, PrCO, EtCO; R1 = CH2CH:CMe2, CH2CH2C(OR2)Me2 (R2 = H, acyl)] were prepd. by known methods and exhibited analgesic activity.
IT **67572-27-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenolysis of)
RN 67572-27-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-benzoyl-3-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

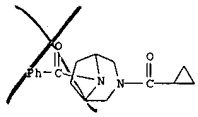


● HCl

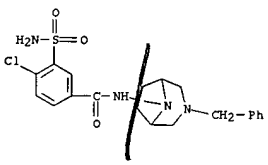
L17 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:593231 CAPLUS
DOCUMENT NUMBER: 83:193231
TITLE: Bicyclic analogs of piperazine. XIII. Derivatives of 3,8-diazabicyclo[3.2.1]octanes with potential antiinflammatory activity
AUTHOR(S): Fontanella, L.; Occelli, E.; Testa, E.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1975), 30(9), 742-53
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI For diagram(s), see printed CA Issue.
AB Diazabicyclooctanes I (R = Me, R2 = acyl; R = carboxyalkyl, acyl, R1 = Me; R = CO2Et, R1 = substituted alkyl, isonicotinoyl; R = H, R1 = cyclopropylmethyl; R = CH2CO2H, R1 = COC6H4Cl-4) (40 compds.) were prepd. by acylation of I (R or R1 = Me) reaction with alkyl chloride, or acylation and redn.
IT **57269-57-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and debenzylation of)
RN 57269-57-5 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3-(cyclopropylmethyl)-8-(phenylmethyl)- (9CI) (CA INDEX NAME)



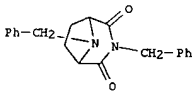
IT **57269-56-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 57269-56-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 8-benzoyl-3-(cyclopropylcarbonyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:539972 CAPLUS
DOCUMENT NUMBER: 77:139972
TITLE: Bicyclic analogs of piperazine. X. N-amino derivatives of 3,8-diazabicyclo[3.2.1]octane, 3,8-diazabicyclo [3.2.1]octane-2,4-diones, and 2,6-dimethylpiperazine with potential pharmacological activity
AUTHOR(S): Fontanella, L.; Occelli, E.; Testa, E.; Cignarella, G.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1972), 27(9), 755-72
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI For diagram(s), see printed CA Issue.
AB The diazabicyclooctanes I [R = NO, H, Me, CH2, Ph, CH2CH:-CHPh, COEt, NH2; R1 = Me, COEt, CO2Et, NO, NH2, NHCOEt, NHCOC6H3(SO2NH2)Cl-3,4 , the diazabicyclooctane-diones II (R = NO, NH2, substituted amino) and some related piperazine derivs. were prepd. for testing for pharmacol. activity. I (R = NHCO2Et, R1 = CH2CH:CHPh) had anticonvulsant, analgesic, and local anesthetic activity and I (R = COEt, R2 = Me, CH2CH:CHPh) also showed some activity. II (R = 3,4-(MeO)2C6H3CH2NH) had slight analgesic activity. The piperazines had considerably lower diuretic activity than Clopamide.
IT **38074-18-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 38074-18-9 CAPLUS
CN Benzamide, 3-(aminosulfonyl)-4-chloro-N-[3-(phenylmethyl)-3,8-diazabicyclo[3.2.1]oct-8-yl]- (9CI) (CA INDEX NAME)

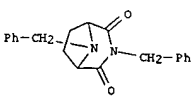


L17 ANSWER 29 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:514359 CAPLUS
DOCUMENT NUMBER: 77:114359
TITLE: Synthesis of N,N'-dibenzylpyrrolidine-2,5-dicarboximide (3,8-diazabicyclo[3.2.1]Octane-2,4-dione)
AUTHOR(S): Della, E. W.; Kendall, M.
CORPORATE SOURCE: Sch. Phys. Sci., Flinders Univ. South Australia, Bedford Park, Australia
SOURCE: Australian Journal of Chemistry (1972), 25(8), 1827-8
CODEN: AJCHAS; ISSN: 0004-9425
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The title compd. (I) was prepd. by cyclizing the pyrrolidine (II, R = H, R1 = PhCH2NH) (III), which was obtained by hydrolysis of the ester prepd. from II (R = Et, R1 = OEt) by the method of S. W. Blackman and R. J. Baltzly (1961). Thus, III was treated with SO2Cl2 to give 75% I.HCl.
IT **17740-41-9P 37061-44-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 17740-41-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 3,8-bis(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

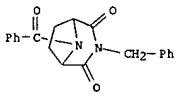


● HCl

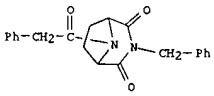
RN 37061-44-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 3,8-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:85788 CAPLUS
DOCUMENT NUMBER: 76:85788
TITLE: Bicyclic homologs of piperazine. XI. 3,8-Diazabicyclo[3.2.1]octane-2,4-diones with potential pharmacological activity
AUTHOR(S): Fontanella, L.; Occelli, E.
CORPORATE SOURCE: Lab. Ric., Gruppo Lepetit S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1972), 27(1), 68-78
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian
GI For diagram(s), see printed CA Issue.
AB The 3-substituted 3,8-diazabicyclo[3.2.1]octane-2,4-diones, I (R = H), are alkylated and acylated and treated with isocyanates to give 3,8-disubstituted compds. I (R = H, R1 = Me) is treated with BuI to give I (R = Bu, R1 = Me). Similarly prepd. are .apprx.30 addnl. I (R = alkyl, acyl, CONH2, CONHPh; R1 = H, Me, PhCH2, aryl). II is treated with NH3 to give I (R = Me, R1 = H); and I (R = H, R1 = p-tolyl) is prepd. by the distn. of III.
IT **35101-50-9 35101-51-0 35101-52-1**
RL: PROC (Process)
(prepn. of)
RN 35101-50-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 8-benzoyl-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

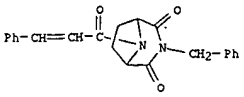


RN 35101-51-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 8-(phenylacetyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

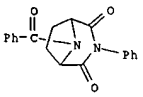


RN 35101-52-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 8-(1-oxo-2-phenyl-2-propenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

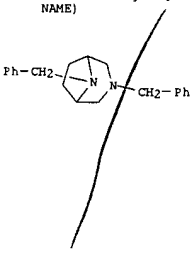
L17 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



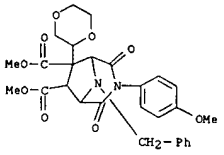
IT **35142-72-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 35142-72-4 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 8-benzoyl-3-phenyl- (9CI) (CA INDEX NAME)



L17 ANSWER 31 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:3795 CAPLUS
DOCUMENT NUMBER: 76:3795
TITLE: Synthesis of 2,5- and 2,6-bis(bromomethyl)-1,4-diphenylpiperazines and their conversion into 2,5-diphenyl-2,5-diazabicyclo[2.2.2]octane
AUTHOR(S): Nelson, David A.; Worman, James J.; Keen, Brian
CORPORATE SOURCE: Dep. Chem., Univ. Wyoming, Laramie, WY, USA
SOURCE: Journal of Organic Chemistry (1971), 36(22), 3361-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Treatment of cis-1,5-diphenyl-3,7 - dihydroxyoctahydro - 1,5 - diazocine with PBr3 yielded a mixt. of cis-2,6-bis(bromomethyl)-1,4-diphenylpiperazine (I) and cis-2,5-bis(bromomethyl)-1,4-diphenylpiperazine (II). The structures of I and II were confirmed by conversion to the corresponding dimethyl-1,4-diphenylpiperazines (III and IV) by LiAlH4. III and IV were synthesized from cis-2,5- and cis-2,6-dimethylpiperazines. Both I and II on treatment with Mg in THF were converted to 2,5-diphenyl-2,5-diazabicyclo[2.2.2]-octane (V). The interconversion of I and II is discussed.
IT **17740-42-0**
RL: PRP (Properties)
(nuclear magnetic resonance spectrum of)
RN 17740-42-0 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3,8-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1970:78780 CAPLUS
DOCUMENT NUMBER: 72:78780
TITLE: Photoinduced 1,3-dipolar cycloaddition reaction of aziridinedicarboximide
AUTHOR(S): Oida, Sadao; Ohki, Eiji
CORPORATE SOURCE: Cent. Res. Lab., Sankyo Co., Ltd., Tokyo, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1969), 17(12), 2461-74
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Cycloaddn. of MeO2CC.tplbond.CCO2Me to N-(p-methoxyphenyl)-1-benzyl-2,3-aziridinedicarboximide was not effected thermally, but under irradn. it gave 3 1:1-cycloadducts and a 1:2-cycloadduct I. The structural detn. of the cycloadducts was via their spectral dataand chem. degradations. Mutual photochem. transformation of the cycloadducts was verified.
IT **25435-24-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 25435-24-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-6,7-dicarboxylic acid, 8-benzyl-6-p-dioxan-2-yl-3-(p-methoxyphenyl)-2,4-dioxo-, dimethyl ester (8CI) (CA INDEX NAME)



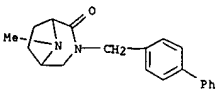
L17 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1969:115125 CAPLUS
DOCUMENT NUMBER: 70:115125
TITLE: Bicyclic homologs of piperazine. VIII. Synthesis and characteristics of 3,8-diazabicyclo[3.2.1]octan-2-ones
AUTHOR(S): Testa, Emilio; Cignarella, Giorgio; Fontanella, Luigi; Occelli, Emilio
CORPORATE SOURCE: Lab. Ric., "Lepetit" S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1969), 24(4), 418-34
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian

AB 3,8-Diazabicyclo[3.2.1]-octan-2-one (I) is prepd. and converted to 3-(R-substituted)-8-(R1-substituted)-3,8-diazabicyclo[3.2.1]octan-2-ones (II). Me cis-1-carbobenzoxy-2-carbamoylpyrrolidine-5-carboxylate (III) (m. 91-2.degree.) is prepd. from the acid. III (250 g.) is heated with 188.1 g. p-MeC6H4SO2Cl in 750 ml. pyridine to give 78% Me cis-1-carbobenzoxy-2-cyanopyrrolidine-5-carboxylate (cis-IV)-trans-IV 1:1 mixt., b0.4 133-5.degree.. IV (6 g.) in 100 ml. HOAc is hydrogenated over 1 g. PtO2 to give 19% I, m. 181-2.degree.; I (49%) is also prepd. in the presence of Raney Ni. I (1 g.) is treated with 1 g. LiAlH4 to give 70% 3,8-diazabicyclo[3.2.1]octane, b35 100.degree.; 2HCl salt m. 114-16.degree.; dipicrate m. 247-9.degree.. A mixt. of 2.6 g. I, 4 ml. 31.7% H2CO, 80 ml. water, and 2.6 g. 10% Pd/C is treated with H2 500 ml. H absorbed after 2 hrs. to give 89% II (R = CH2OH, R1 = Me) (V), b0.6 145.degree., citrate m. 138-40.degree.. A mixt. of 126 g. I, 126 ml. 31.5% H2CO, 250 ml. EtOH, and 126 g. 10% Pd/C is treated with H2 20 l. H is absorbed after 0.5 hr. to give 116 g. II (R = H, R1 = Me), m. 96-7.degree. (HCl salt m. 280-2.degree.), and 8 g. V. II (R = H, R1 = Me) (5 g.) is treated with 5.4 ml. 30% H2CO and 7.3 g. Et2NH to give 87% 3-(diethylaminomethyl)-8-methyl-3,8-diazabicyclo[3.2.1]octan-2-one, b0.8 144-6.degree.. Similarly prepd. are the following II (R1 = Me) (R and b.p./mm. given): 3,4,5-trimethylpiperazinomethyl, 158-60.degree./0.7; 8-propionyl-3,8-diazabicyclo[3.2.1]oct-3-ylmethyl, -. Also prepd., according to known methods, are the following II (R, R1, b.p./mm., and m.p. given): H, cyclohexylmethoxycarbonyl, -, 160-1.degree.; H, CO2CH2Ph, -, 100-1.degree.; COEt, COEt, -, 102-4.degree.; H, COEt, 180.degree./0.8, -; Me, COEt, 165-70.degree./0.8, 38-40.degree.; CH2CH:CHPh, COEt, 235-40.degree./0.8, -; CH2CH:CMe2, COEt, 162-5.degree./0.6, -; Bz, Me, -, 130-2.degree.; p-ClC6H4CO, Me, -, 143-4.degree.; L-.alpha.-methyltropoyl, Me, -, 240-3.degree., [.alpha.]20D 9.3.degree. (water): CH2CH:CHPh, Me, 194-6.degree./0.8, -; allyl, Me, 130.degree./0.8, -; p-PhC6H4CH2, Me, -, 118.degree.; propargyl, Me, 130.degree./0.8, -; H, p-PhC6H4CH2, -, 150-2.degree.; Me, p-PhC6H4CH2, -, -(methiodide m. 183-4.degree.); I.HCl, m. 262-5.degree.; I picrate, m. 210-12.degree..

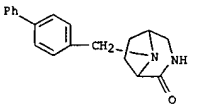
IT **22315-33-9P 22315-35-1P 22315-36-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 22315-33-9 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-methyl-3-(p-phenylbenzyl)- (8CI) (CA INDEX NAME)

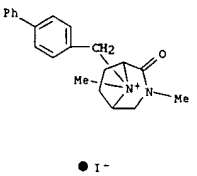
L17 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



RN 22315-35-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octan-2-one, 8-(p-phenylbenzyl)- (8CI) (CA INDEX NAME)



RN 22315-36-2 CAPLUS
CN 3-Aza-8-azoniabicyclo[3.2.1]octane, 3,8-dimethyl-2-oxo-8-(p-phenylbenzyl)-, iodide (8CI) (CA INDEX NAME)



● I⁻

L17 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1968:49651 CAPLUS
DOCUMENT NUMBER: 68:49651
TITLE: 3,8-Disubstituted-3,8-diazabicyclo[3.2.1]octanes
INVENTOR(S): Kirchner, Frederick K.
PATENT ASSIGNEE(S): Sterling Drug Inc.
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3328396		19670627	US	19611109

GI For diagram(s), see printed CA Issue.

AB Thus, 0.1 mole diethyl 1-methyl-2,5-pyrrolidinedicarboxylate (II) was heated to 150.degree. and 0.1 mole benzylamine added during 15 min. After increasing the temp. to 180.degree., EtOH, began to distil. The temp. was increased to 280.degree. during 2 hrs. and 7.2 cc. EtOH was collected to give 3-benzyl-2,4-dioxo-3-methyl-3,8-diazabicyclo[3.2.1]octate, m. 100.0-4.4.degree. (hexane) (procedure A). The picrate m. 175-8.degree. (decompn.) (EtOH). LiAlH4 redn. of the dioxo compd. in Et2O gave I (R = PhCH2, R1 = Me) (III), b9.2 84-94.degree., n25D 1.5368 (procedure B). Refluxing 2.0 g. III in Et2O with excess MeI 1 hr. gave the methiodide, m. 245.0-8.2.degree. (EtOH) (procedure C). III (10 g.) in 400 cc. EtOH was acidified with concd. HCl and hydrogenated over Pd/C 6 hrs. at 23.degree. and 45 psi. to give I.2 HCl (R = H, R1 = Me) (IV), m. 325.degree. (decompn.) (procedure D). By these procedures were prepd. 3-(3,4-dichlorobenzyl)-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane, m. 103.6-8.6.degree. (abs. EtOH), from II and 3,4-dichlorobenzylamine; I.2HCl (R = 3,4-Cl2C6H3CH2, R1 = Me), m. 216.4-20.8.degree. and its ethobromide; 3-(4-dimethylaminobenzyl)-2,4-dioxo-8-methyl-3,8-diazabicyclo[3.2.1]octane [the di-HCl salt m. 236.8.degree. (decompn.) (dry MeOH)]; I (R = p-Me2NC6H4CH2, R1 = Me); 3-(4-chlorobenzyl)-2,4-dioxo-8-methyl-3,8-diazabicyclo[3.2.1]octane, m. 103.0-10.4.degree. (abs. EtOH); I.2HCl (R = p-ClC6H4CH2, R1 = Me), m. 234.0-7.2.degree. and its N-benzyl chloride; 2,4-dioxo-8-methyl-3-phenethyl-3,8-diazabicyclo[3.2.1]octane HCl salt, m. 205.6-10.8.degree.; I.2HCl (R = PhCH2CH2, R1 = Me), m. 245.degree. (decompn.) and its methosulfate; 3-(3,4-dimethoxybenzyl)-2,4-dioxo-8-methyl-3,8-diazabicyclo[3.2.1]octane HCl salt, m. 228.degree. (decompn.); I.2HCl [R = 3,4-(MeO)2C6H4CH2, R1 = Me], m. 194.4.degree. (decompn.) and the quaternary salt with allyl bromide. To 0.80 mole benzylamine, 0.267 mole diethyl .alpha.,.alpha.'-dibromoadipate (V) was added with ice cooling. After warming to room temp., a vigorous reaction started and was controlled by cooling followed by heating at 95.degree.. The cryst. product was taken up in 5 N H2SO4, extd. with Et2O basified with solid NaHCO3, extd. with Et2O, the solvent evapd. in vacuo, and the residual oil distd. to give 1-benzyl-2,5-dicarbethoxypyrrolidine, b14 210-16.degree. (procedure E). Using procedure A, 0.05 mole of the above compd. was treated with 0.056 mole benzylamine to give 3,8-dibenzyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane HCl salt, m. 192.4.degree.. Using procedure B, the above free base was reduced to I (R = R1 = PhCH2) (VI), m. 58.6-60.4.degree. (aq. EtOH). Using procedure C, VI was converted to the methiodide. Using excess MeI produced the bismethiodide. Using procedure D, VI was hydrogenated to give I.2HCl (R = R1 = H), m. >300.degree. (abs. MeOH). Also, 0.027 mole IV and 0.027 mole .alpha.-acetoxymethylphenylacetyl chloride (VII) were added to a soln. contg. 0.08 mole NaOH in 50 cc. H2O and the mixt. kept cool overnight to

L17 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

give 3-(3-acetoxy-2-phenylpropionyl)-8-methyl-3,8-diazabicyclo[3.2.1]octane hydrochloride (procedure F). To a soln. contg. 0.014 mole of the above salt in 50 cc. abs. MeOH, 4 cc. 4N aq. HCl was added and the soln. kept at room temp. several days. Addn. of a large amt. of abs. Et2O caused the pptn. of a white gum which solidified in abs. EtOH to give 3-(3-hydroxy-2-phenylpropionyl)-8-methyl-3,8-diazabicyclo[3.2.1]octane hydrochloride, m. 195.3-203.3.degree. (abs. EtOH-abs. Et2O). This compd. had 15.5% of the activity of atropine sulfate in the mouse after s.c. injection. The LD50 in mice was 160 .+-. 12 mg./kg.i.v. A soln. of 0.04 mole IV in 100 cc. dry Et2O was added dropwise over 2 hrs. to a well-stirred soln. of 0.04 mole ethanesulfonyl chloride in 100 cc. dry Et2O to give I.HCl (R = EtSO2, R1 = Me), m. 261.2-4.6.degree. (decompn.) (MeOH). IV (0.039 mole free base) was added cautiously with cooling to 15 cc. 100% HCO2H and 0.04 mole 37% HCHO. The mixt. was heated at 95.degree. overnight, 9 cc. concd. HCl added, and the mixt. heated 3 hrs. at 95.degree. to give I.HCl (R = R1 = Me), m. 273.2-7.4.degree. (decompn.) (EtOH). Using procedure F, 0.04 mole IV was treated with 0.04 mole VII. The acetoxy group was hydrolyzed with dil. NaOH to give 3-(.alpha.-hydroxyphenylacetyl)-8-methyl-3,8-diazabicyclo[3.2.1]octane hydrochloride, m. 226.4-7.8.degree.. Using procedure F, 0.03 mole IV was treated with 0.03 mole BzCl to give I.HCl (R = Bz, R1 = Me), m. 264.4-7.6.degree. (abs. MeOH-Et2O). To a soln. contg. 0.012 mole of the above salt in 100 cc. abs. MeOH, 1.7 g. dry K2CO3 and 5 cc. MeI were added and the mixt. was refluxed overnight to give I.MeI (R = Bz, R1 = Me), m. 235-8.degree.. A soln. of the methiodide in 100 cc. H2O was poured through a column of a Cl- exchange resin to give I.MeCl (R = Bz, R = Me), m. 239-40.6.degree. (decompn.) (procedure G). I (R = 3-indolylmethyl, R1 = Me), m. 153.8-7.60, was prepd. from 0.03 mole IV, 2.44 g. 37% HCHO, 0.03 mole indole, and 6 cc. AcOH. Excess NaOH was added to a soln. contg. 0.03 mole IV in 5 cc. H2O and the free base extd. into 200 cc. C6H6, 0.02 mole 4-chlorobenzhydryl isothiocyanate in 50 cc. C6H6 added, and the soln. refluxed 1.5 hrs. to give 3-(4-chlorobenzyhydrylthiocarbamoyl)-8-methyl-3,8-diazabicyclo[3.2.1]octane, m. 123.6-7.2.degree.. To a suspension of 0.12 mole IV in 60 cc. C6H6, 10 cc. 35% aq. NaOH was added. After stirring, the org. phase was sepd. and the aq. phase extd. with C6H6, the C6H6 ext. dried, and 0.02 mole diphenylchloroacetyl chloride added dropwise with stirring to give I.HCl (R = ClCPh2CO, R1 = Me), m. 248-50.degree. (decompn.) (procedure H). The above salt (5 g.) dissolved in H2O was basified with 10% Na2CO3 soln. to give I (R = HOCPh2CO, R1 = Me), m. 193.6-200.6.degree.. Similarly was prepd. I.HCl (R = Ph2CHCO, R1 = Me), m. 278.2-81.75.degree. (decompn.). To a suspension contg. 0.3 mole IV in 300 cc. C6H6, 0.7 mole NaOH and 30 cc. H2O was added. After stirring, the C6H6 phase was dried, the solvent evapd., the resultant free base dissolved in 50 cc. abs. EtOH, the soln. cooled in ice, 0.35 mole ethylene oxide in 50 cc. EtOH added, and the soln. warmed to room temp. and kept overnight to give I (R = HOCH2CH2, R1 = Me) (VIII), b0.4 89-90.degree.; di-HCl salt m. 239.4-240.8.degree. (decompn.). Using procedure A, 15 g. o-chlorobenzylamine was treated with 0.1 mole II to give 3-(2-chlorobenzyl)-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane hydrochloride, m. 250.0-1.6.degree. (decompn.) (abs. MeOH). Using procedure B, the base corresponding to the above salt was reduced to give I (R = o-ClC6H4CH2, R1 = Me). To a soln. of 0.02 mole VIII in 20 cc. dry C6H6, 0.02 mole phenyl isocyanate was added, the soln. brought to reflux and let cool. Excess ethereal HCl was added and the resulting gum crystd. from abs. EtOH to give 3-(2-carbanilinoxyethyl)-8-methyl-3,8-diazabicyclo[3.2.1]octane as the dihydrochloride with an indefinite m.p. but softening at 176.8.degree.. To a soln. of 0.02 mole VIII and 0.02 mole NaOH in 20 cc. H2O, 0.02 mole BzCl was added dropwise, the mixt. shaken thoroughly while ice cooled, and extd. with Et2O.

L17 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

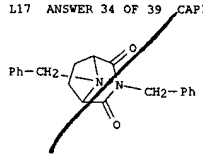
Ethereal HCl was added to the dried Et2O ext. to give I.2HCl (R =BzOCH2CH2, R1 = Me), m. 197.2-209.6.degree. (decompn.). This compd. had 1.1 times the local anesthetic activity of procaine in guinea pigs. The i.v. LD50 in mice was 28 .+-. 1.6 mg./kg. Using procedure E, 1.0 mole 3-diethylaminopropylamine was treated with 0.5 mole V in 700 cc. C6H6 to give 1-(3-diethylaminopropyl)-2,5-dicarbethoxypyrrolidine (IX), b0.5 135-40.degree., n25D 1.4588. Using procedure A, 0.1 mole IX was treated with 0.1 mole benzylamine to give 3-benzyl-8-(3-diethylaminopropyl)-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane as the HCl salt, m. 183.0-194.8.degree. (abs. EtOH). The salt had twice the local anesthetic activity of procaine in guinea pigs. The i.v. LD50 in mice was 31 mg./kg. Using procedure B, the free base corresponding to the above salt was reduced to give I (R = PhCH2, R1 = Et2N(CH2)3]. Using procedure A, 6.5 g. diethylaminopropylamine was treated with 0.05 mole II to give 3-(3-diethylaminopropyl)-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane hydrochloride, m. 209.2-12.2.degree. (abs. EtOH). Using procedure B, the above salt was reduced to give I [R = Et2N(CH2)3, R1 = Me], b3.5 126-30.degree., n25D 1.4782; tri-HCl salt m. 169-71.degree.. Using procedure G, 0.01 mole of the above base was treated with 15 cc. MeI and 0.017 mole K2CO3 in 100 cc. abs. MeOH to give 3-(3-diethylaminopropyl)-8-methyl-3,8-diazabicyclo[3.2.1]octane bismethiodide, m. 263.4-6.4.degree. (decompn.). Using procedure A, 0.1 mole II was treated with 0.1 mole diethylaminoethylamine to give 3-(2-diethylaminoethyl)-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane dihydrochloride, m. 221.0-2.8.degree. (decompn.). Using procedure B, the free base corresponding to the above di-HCl salt was reduced to give I.3HCl (R = Et2NCH2CH2, R1 = Me), m. 225.6-33.2.degree. (decompn.). Using procedure A, 0.1 mole II was treated with 0.1 mole 4-diethylaminobutylamine to give 3-(4-diethylaminobutyl)-8-methyl-2,4-dioxo-3,8-diazabicyclo[3.2.1]octane dehydrochloride, m. 194.6-6.2.degree. (decompn.). Using procedure B, the above free base was reduced to give I [R = Et2N(CH2)4, R1 = Me]. Using procedure A, 11.5 g. II was treated with 0.05 mole 10-(3-aminopropyl)phenothiazine to give 8-methyl-2,4-dioxo-3-[3-(10-phenothiazinyl)propyl]-3,8-diazabicyclo[3.2.1]octane, m. 133.4-7.2.degree. (95% EtOH). Using procedure B, the above base was reduced to give I.2HCl [R =3-(10,phenothiazinyl)propyl), R1 = Me], m. 136.2.degree. but softened at 118.0 (abs. EtOH).

IT **17740-41-9P 17740-42-0P 17783-47-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 17740-41-9 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 3,8-bis(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

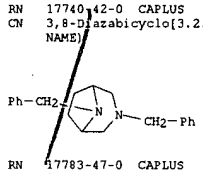
L17 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



● HCl

RN 17740-42-0 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane, 3,8-bis(phenylmethyl)- (9CI) (CA INDEX NAME)

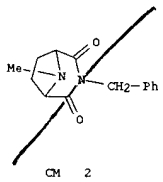


RN 17783-47-0 CAPLUS

CN 2,5-Pyrrolidinedicarboximide, N-benzyl-1-methyl-, picrate (8CI) (CA INDEX NAME)

CM 1

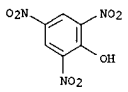
CRN 17783-46-9
CMF C14 H16 N2 O2



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7

L17 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)



L17 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1964:425460 CAPLUS
DOCUMENT NUMBER: 61:25460
ORIGINAL REFERENCE NO.: 61:4374a-g
TITLE: Diazabicyclooctane derivatives
INVENTOR(S): Lepetit, S.p.A.
SOURCE: 12 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 633541		19631104	BE	
FR 1365537			FR	
GB 988526			GB	

PRIORITY APPLN. INFO.: GB 19620615

GI For diagram(s), see printed CA Issue.

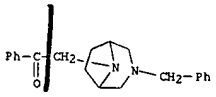
AB Improved routes to certain 3- and 8-substituted derivs. of I are described. Thus, a mixt. of 6.7 g. 3-benzyl-3,8-diazabicyclo(3.2.1)octane (II), and 12.8 g. (EtCO)2O was heated 1.5 hrs. at 100.degree., cooled, acidified with HCl, extd. with Et2O (discarded), the aq. layer alkalized at -5.degree., and the sepd. oil extd. into Et2O. Fractionation of the ext. gave 7.4 g. 3-benzyl-8-propionyl-3,8-diazabicyclo(3.2.1)octane (III), b1 174.degree., b0.4 133-7.degree.. III was hydrogenated in 60 cc. EtOH with 3 g. 10% Pd-C at 60.degree. and 50 atm. to give 4.3 g. 8-propionyl-3,8-diazabicyclo(3.2.1)octane (IV), b0.1 121.degree.. A mixt. of 0.05 mole IV in 100 cc. Me2CO and 0.6 mole K2CO3 was stirred and treated with 0.06 mole PhCH:CHCOCl in 40 cc. Me2CO, refluxed 7 hrs., concd., the residue dissolved in 10% HCl and the soln. extd. with Et2O (discarded). The aq. layer was alkalized, the sepd. base extd. into Et2O, and the ext. fractionated, to give 3-cinnamyl-8-propionyl-3,8-diazabicyclo(3.2.1)octane (V), b0.2 170.degree.. The following 8-propionyl derivs. were similarly prepd. (3-substituent and b.p./mm. or m.p. given): Et 85-90.degree./0.4; iso-Pr 100.degree./0.2; Bu 105.degree./0.2; allyl 95-8.degree./ 0.2; phenylethyl 150.degree./0.3; cyclopentylmethyl 133-8.degree./0.3; cyclopentylethyl 145.degree./0.4; phenylpropyl 175.degree./0.47; p-methoxycinnamyl 150.degree./0.1; Ph 86-8.degree.; p-nitrocinnamyl 220.degree.; p-chlorocinnamyl 220-3.degree.; o-chlorocinnamyl 201-4.degree.; p-methyldinnamyl 66-8.degree.; naphthylallyl 160-5.degree.; m-chlorocinnamyl 203-5.degree.. A soln. of 2.3 g. II in 10 cc. 2N NaOH was treated dropwise at -5.degree. with 1.92 g. BzCl, the mixt. stirred 3 hrs. at room temp., dild. with H2O, and extd. with Et2O. The ext. left 2.9 g. of viscous oil, which was treated with alc. HCl to give 3 g. HCl salt of the 3-benzyl-8-benzoyl deriv. of I, m. 219-21.degree. (EtOH). The free base, hydrogenated as described for III, gave 1.5 g. 8-benzoyl-3,8-diazabicyclo(3.2.1)octane (VI), b0.5 140-2.degree.; m. 82-3.degree. (Et2O). Similarly prepd. were the 3-benzyl-8-phenacyl (m. 78-81.degree.) and 3-benzyl-8-butyryl (m. 65-6.degree.) derivs. of I. IV was converted into its 3-propionyl isomer (VII) in 3 ways: (1) 1 g. IV was heated 5 hrs. at 120.degree. and distd. to yield 0.8 g. VII, b0.2 128-30.degree., m.p. and mixed m.p. 38-40.degree. (sublimes); (2) 1 g. IV was dissolved in 5 cc. 2N NaOH contg. a little alc., allowed to stand 4 hrs. at room temp., concd. in vacuo, and extd. with Et2O; the ext. gave 0.5 g. oil with properties as above; (3) 1 g. IV was dissolved in 10 cc. abs. alc., the soln. satd. with HCl, refluxed 2 hrs. in a current of HCl, cooled, and filtered from 0.36 g. of the 2HCl salt of I (identified by mixed m.p. and infrared spectrum). The filtrate was evapd. in vacuo, the residue alkalized with 20% alc. NH3, Et2O added, and NH4Cl filtered off; fractionation of the filtrate gave

L17 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
0.58 g. oil with properties as above. To methylate VII, a soln. of 0.84 g. in 0.7 cc. HCO2H and 0.79 g. 38% CH2O was refluxed 15 hrs., cooled, treated with 1 cc. HCl, concd. in vacuo, alkalized, extd. with Et2O, and the ext. fractionated to give 0.54 g. 3-propionyl-8-methyl deriv. of I, bl 110-12.degree.. VII was benzylated as described for IV to V to give the 3-propionyl-8-benzyl deriv. of I, b0.2 155.degree.. VI was converted into its 3-Bz isomer [m. 122-3.degree. (Et2O)] by the 3 methods described for IV to VII.

IT **100105-97-3**, Acetophenone, 2-(3-benzyl-3,8-diazabicyclo[3.2.1]oct-8-yl)-
(prepn. of)

RN 100105-97-3 CAPLUS

CN Acetophenone, 2-(3-benzyl-3,8-diazabicyclo[3.2.1]oct-8-yl)- (7CI) (CA INDEX NAME)

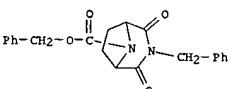


L17 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
di-HCl salt m. 218-20.degree.; Ph, H, b0.2 114.degree.; benzyl, H, b. 95-7.degree.; di-HCl salt m. 145-8.degree.; dipicrate m. 232-5.degree.; H, H, b. 173-5.degree.; di-HCl salt m. 314-15.degree.; dipicrate m. 248-50.degree.. These compds. are pharmacologically active as diuretic, hypotensive, antihistaminic, tranquillizing, and ganglionic blocking agents.

IT **96000-95-2**, 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-benzyl-2,4-dioxo-, benzyl ester
(prepn. of)

RN 96000-95-2 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-benzyl-2,4-dioxo-, benzyl ester (6CI, 7CI) (CA INDEX NAME)



L17 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1964:23448 CAPLUS
DOCUMENT NUMBER: 60:23448
ORIGINAL REFERENCE NO.: 60:4161g-h,4162a-d
TITLE: 3,8-Diazabicyclo[3.2.1]octanes
INVENTOR(S): Cignarella, Giorgio
PATENT ASSIGNEE(S): Lepetit S.p.A.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 937184		19630918	GB	19600217

GI For diagram(s), see printed CA Issue.

AB The title compds. are represented by (I) wherein R is H or an alkyl (C1-8), an aryl, or an arylalkyl group, and X is H or carbobenzyloxy. The process used consists in adding to the internal anhydride of an N-substituted pyrrolidine-2,5-dicarboxylic acid an excess of an amine RNH2 and refluxing the obtained crude monamine with Ac2O. Thus, a soln. of 60 g. 2,5-dicarbethoxy-N-benzylpyrrolidine was hydrogenated at 40.degree./20 atm. in abs. EtOH over 10% Pd-C to give 38 g. 2,5-dicarbethoxypyrrolidine (II), b0.3 95-6.degree.. A suspension of 200 g. II in 8 l. H2O was refluxed for 25-30 hrs. to give 110 g. pyrrolidine-2,5-dicarboxylic acid (III), m. 260-1.degree.. To a soln. of 67 g. III in 420 ml. 2N NaOH soln. cooled to 8-10.degree., 73 g. benzyl chlorocarbonate with 210 ml. 2N NaOH soln. was added with vigorous stirring during 30 min. After 2 hrs. stirring, the soln. yielded 86.5 g. N-carbobenzyloxy-pyrrolidine-2,5-dicarboxylic acid (IV), m. 125-7.degree.. A soln. of 79 g. IV in 360 ml. Ac2O was refluxed 1 hr. to give 58.1 g. IV anhydride (V), m. 166-8.degree.. To a soln. of 27.5 g. V in 300 ml. anhyd. C6H6 a soln. of 1.9 g. NH3 in 50 ml. C6H6 was added with cooling. The mixt. was refluxed for 30 min., the solvent removed, and the resulting monamide refluxed with Ac2O 1 hr. at 130-40.degree. under 1 atm. pressure to give 18 g. 8-carbobenzyloxy-3,8-diazabicyclo[3.2.1]octane-2,4-dione (I, X = PhCH2O2C, R = H) (VI), m. 125.degree.. Similarly prepd. I (X = PhCH2O2C) analogs were (R and b.p. given): Me, b0.3 170-2.degree.; Bu, b0.3 192-4.degree.. Also prepd. were I (R, X, and m.p. given): Ph, CO2CH2Ph, 148-9.degree.; benzyl, CO2CH2Ph, 83-4.degree.; Me, H, 105-7.degree.; H, H, 223-6.degree.; benzyl, H, 78.degree. (b0.2 150-2.degree.). A mixt. of 21.5 g. II and 11.8 g. PhCH2NH2 in 50 ml. dry Me2C6H4 was refluxed for 24 hrs. to give 20.2 g. 2-carbethoxy-5-benzylcarbamoylpyrrolidine (VII), b0.3 178-80.degree.. Mild warming of 20.2 g. VII gave 16.5 g. 3-benzyl-3,8-diazacyclo[3.2.1]octane-2,4-dione, b0.2 150-2.degree.. A soln. of 27.4 g. VI was added dropwise, with stirring, to an Et2O suspension of 5.7 g. LiAlH4 at 0-5.degree.. The mixt. was then brought to room temp. and refluxed for 3-4 hrs. to give 8-methyl-3,8-diazabicyclo[3.2.1]octane (VIII, X = Me, R = H), b. 163-5.degree.; MeI salt m. 225-7.degree.; di-HCl salt m. 314-15.degree.; dipicrate m. 252-4.degree.. Similarly prepd. VIII were (R, X, b.p. and m.ps. salts if prepd. given): Me, Me, b8 50-2.degree., MeI salt m. 314-15.degree.; dipicrate m. 220-2.degree.; Ph, Me, b0.2 105-8.degree.; cinnamyl, Me, b0.6 120-30.degree.; p-chlorobenzhydryl, Me, -; HCl salt m. 176-9.degree.; o-chlorobenzhydryl, Me, -; di-HCl salt m. 283-7.degree.; benzyl, Me, -;

L17 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1964:23447 CAPLUS
DOCUMENT NUMBER: 60:23447
ORIGINAL REFERENCE NO.: 60:4161g-h,4162a-d
TITLE: 3,8-Diazabicyclo[3.2.1]octanes
INVENTOR(S): Cignarella, Giorgio
PATENT ASSIGNEE(S): Lepetit S.p.A.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 937183		19630918	GB	19600217
DE 1200316			DE	
US 3221015		1965	US	

GI For diagram(s), see printed CA Issue.

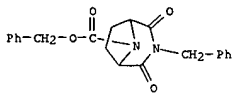
AB The title compds. are represented by (I) wherein R is H or an alkyl (C1-8), an aryl, or an arylalkyl group, and X is H or carbobenzyloxy. The process used consists in adding to the internal anhydride of an N-substituted pyrrolidine-2,5-dicarboxylic acid an excess of an amine RNH2 and refluxing the obtained crude monamine with Ac2O. Thus, a soln. of 60 g. 2,5-dicarbethoxy-N-benzylpyrrolidine was hydrogenated at 40.degree./20 atm. in abs. EtOH over 10% Pd-C to give 38 g. 2,5-dicarbethoxypyrrolidine (II), b0.3 95-6.degree.. A suspension of 200 g. II in 8 l. H2O was refluxed for 25-30 hrs. to give 110 g. pyrrolidine-2,5-dicarboxylic acid (III), m. 260-1.degree.. To a soln. of 67 g. III in 420 ml. 2N NaOH soln. cooled to 8-10.degree., 73 g. benzyl chlorocarbonate with 210 ml. 2N NaOH soln. was added with vigorous stirring during 30 min. After 2 hrs. stirring, the soln. yielded 86.5 g. N-carbobenzyloxy-pyrrolidine-2,5-dicarboxylic acid (IV), m. 125-7.degree.. A soln. of 79 g. IV in 360 ml. Ac2O was refluxed 1 hr. to give 58.1 g. IV anhydride (V), m. 166-8.degree.. To a soln. of 27.5 g. V in 300 ml. anhyd. C6H6 a soln. of 1.9 g. NH3 in 50 ml. C6H6 was added with cooling. The mixt. was refluxed for 30 min., the solvent removed, and the resulting monamide refluxed with Ac2O 1 hr. at 130-40.degree. under 1 atm. pressure to give 18 g. 8-carbobenzyloxy-3,8-diazabicyclo[3.2.1]octane-2,4-dione (I, X = PhCH2O2C, R = H) (VI), m. 125.degree.. Similarly prepd. I (X = PhCH2O2C) analogs were (R and b.p. given): Me, b0.3 170-2.degree.; Bu, b0.3 192-4.degree.. Also prepd. were I (R, X, and m.p. given): Ph, CO2CH2Ph, 148-9.degree.; benzyl, CO2CH2Ph, 83-4.degree.; Me, H, 105-7.degree.; H, H, 223-6.degree.; benzyl, H, 78.degree. (b0.2 150-2.degree.). A mixt. of 21.5 g. II and 11.8 g. PhCH2NH2 in 50 ml. dry Me2C6H4 was refluxed for 24 hrs. to give 20.2 g. 2-carbethoxy-5-benzylcarbamoylpyrrolidine (VII), b0.3 178-80.degree.. Mild warming of 20.2 g. VII gave 16.5 g. 3-benzyl-3,8-diazacyclo[3.2.1]octane-2,4-dione, b0.2 150-2.degree.. A soln. of 27.4 g. VI was added dropwise, with stirring, to an Et2O suspension of 5.7 g. LiAlH4 at 0-5.degree.. The mixt. was then brought to room temp. and refluxed for 3-4 hrs. to give 8-methyl-3,8-diazabicyclo[3.2.1]octane (VIII, X = Me, R = H), b. 163-5.degree.; MeI salt m. 225-7.degree.; di-HCl salt m. 314-15.degree.; dipicrate m. 252-4.degree.. Similarly prepd. VIII were (R, X, b.p. and m.ps. salts if prepd. given): Me, Me, b8 50-2.degree., MeI salt m. 314-15.degree.; dipicrate m. 220-2.degree.; Ph, Me, b0.2 105-8.degree.; cinnamyl, Me, b0.6 120-30.degree.; p-chlorobenzhydryl, Me, -; HCl salt m. 176-9.degree.; o-chlorobenzhydryl, Me, -; di-HCl salt m. 283-7.degree.; benzyl, Me, -; di-HCl salt m. 218-20.degree.; Ph, H, b0.2 114.degree.; benzyl, H, b. 95-7.degree.; di-HCl salt m. 145-8.degree.; dipicrate m. 232-5.degree.; H,

L17 ANSWER 37 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
H, b. 173-5.degree.; di-HCl salt m. 314-15.degree.; dipicrate m. 248-50.degree.. These compds. are pharmacologically active as diuretic, hypotensive, antihistaminic, tranquillizing, and ganglionic blocking agents.

IT **96000-95-2**, 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-benzyl-2,4-dioxo-, benzyl ester
(prepn. of)

RN 96000-95-2 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-benzyl-2,4-dioxo-, benzyl ester (6CI, 7CI) (CA INDEX NAME)



L17 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1961:144227 CAPLUS

DOCUMENT NUMBER: 55:144227

ORIGINAL REFERENCE NO.: 55:27331g-i,27332a-e

TITLE: Synthesis of 3,8-diazabicyclo[3.2.1]octane and some of its N-substituted derivatives

AUTHOR(S): Blackman, Samuel W.; Baltzly, Richard

CORPORATE SOURCE: Polytech. Inst. of Brooklyn, Brooklyn, NY

SOURCE: Journal of Organic Chemistry (1961), 26, 2750-5
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

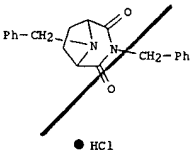
AB The prepn. of 3,8-diazabicyclo[3.2.1]octane (I) and some of its simple N-substituted derivs. was described. Adipoyl chloride brominated by a standard method and added to MeOH gave (overnight) 30% di-Me .alpha.,.alpha.'-dibromoadipate (II), m. 75-6.degree. (MeOH). The original mother liquors and the filtrate from the crystn. of II were collected and the residual ester distd. In some runs, a considerable amt. of the monobromo ester was isolated as a forerun, b16, 155-70.degree.. The main fraction of II b16 170-81.degree.. Recrystn. raised the yield of cryst. II to 30%. II (111 g.) in 250 cc. C6H6 and 250 cc. MeNO2 refluxed 16 hrs. with 124 g. PhNH2 and 1 g. KI gave 27 g. crystals (two types of crystals were present, long orange-yellow needles and clusters of colorless crystals). Mechanical sepn. gave 13 g. trans-dimethyl N-phenylpyrrolidine-2,5-dicarboxylate (III), m. 88.5.degree. (Et2O-hexane); purification by chromatography on Al2O3 gave 44 g. cis-ester (IV) and 13 g. III. In another run, distn. was omitted; the residue dissolved in C6H6-hexane gave 67 g. mixt.; chromatography gave 14 g. III and 44 g. IV. IV (88 g.) in 500 cc. (CH2OH)2 was heated with 40 g. PhCH2NH2 and NaOMe (72 cc. MeOH collected in the first 2 hrs.), heating increased, the mixt. refluxed 16 hrs., the fractionating column removed, and volatile material removed in vacuo. Distn. of the residue gave 38.7 g. 3-benzyl-8-phenyl-3,8-diazabicyclo[3.2.1]octane-2,4-dione (V), m. 166.5.degree. (Me2CO). 8-Phenyl-3,8-diazabicyclo[3.2.1]octane-HCl (2.25 g.) benzoylated by the Schotten-Baumann procedure gave 1.8 g. 3-benzoyl-8-phenyl-3,8-diazabicyclo[3.2.1]octane (VI), m. 131-2.degree.. meso-II (222 g.) in 800 cc. C6H6 stirred 24 hrs. at room temp. with 225 cc. PhCH2NH2, the mixt. refluxed 8 hrs., cooled, and treated with Et2O, the pptd. PhCH2NH2.HBr removed, the combined filtrates extd. with cold dil. H2SO4, and the base liberated with Na2CO3 and extd. with Et2O gave 126 g. dimethyl N-benzylpyrrolidine-2,5-dicarboxylate (VII), b1 148-52.degree.. VII (74 g.), 30 g. PhCH2NH2, 500 cc. (CH2OH)2, and NaOMe (from 5 g. Na) gave 59 g. 3,8-dibenzyl-3,8-diazabicyclo[3.2.1]octane-2,4-dione(VIII), b1 205-11.degree.. VIII (from 8.9 g. of the HCl salt) added dropwise to 15.2 g. LiAlH4 in 1 l. Et2O, the mixt. stirred 30 hrs., excess 10% NaOH added, the mixt. stirred overnight, and the product sepd. gave 5.5 g. 3,8-dibenzyl-3,8-diazabicyclo[3.2.1]octane (IX), m. 52-7.degree. (pentane). IX (5.15 g.) in 50 cc. MeOH contg. 5 cc. satd. MeOH-HCl reduced with 6 g. 10% Pd-C and H gave 2.90 g. I.2HCl monohydrate. I was further characterized as the dipicrate. VIII (9.3 g.) in MeOH hydrogenated over Pd-C gave 6.2 g. 3-benzyl-3,8-diazabicyclo[3.2.1]octane-2,4-dione-HCl (X), m. 216-18.degree.. Free X (6.7 g.) benzoylated by the Schotten-Baumann method and crystd. gave 3-benzyl-8-benzoyl-3,8-diazabicyclo [3.2.1]-octane-2,4-dione (XI), m. 121-3.degree. (with frothing). XI (2 g. reduced by refluxing 24 hrs. with 2 g. LiAlH4 in Et2O gave) 1 g. IX. 3-Benzyl-8-ethyl-3,8-diazabicyclo[3.2.1]octane-2HCl (m.

L17 ANSWER 38 OF 39 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
233.degree.) (7 g.) in 50 cc. MeOH hydrogenated over 6 g. 10% Pd-C in 1.5 min. gave 93% 8-ethyl-3,8-diazabicyclo-[3.2.1]octane, m. 275.degree. (decompn.) (MeOH) as the di-HCl salt (XII). XII (4.3 g.) in 25 cc. Ac2O and 3 g. K2CO3 heated, 12 cc. Ac2O added, refluxing continued, 5 g. K2CO3 added, the mixt. refluxed a few more min., cooled, MeOH added, the mixt. evapd., the residue dild. with H2O, concd. KOH added, and the soln. extd. with C6H6 gave 0.2 g. oil. The ext. was dissolved in 20 cc. hexane and refrigerated; no solid formed, and hence the material was converted to 67% HCl salt of 3-acetyl-8-ethyl-3,8-diazabicyclo[3.2.1]-octane, m. 229-30.degree..

IT **17740-41-9**, 2,5-Pyrrolidinedicarboxiimide, N,1-dibenzyl-, hydrochloride **17740-42-0**, 3,8-Diazabicyclo[3.2.1]octane, 3,8-dibenzyl- **35101-50-9**, 2,5-Pyrrolidinedicarboximide, 1-benzoyl-N-benzyl- **102080-93-3**, 3,8-Diazabicyclo[3.2.1]octane, 3-benzoyl-8-phenyl- **102163-86-0**, 3,8-Diazabicyclo[3.2.1]octane, 3-benzyl-8-phenyl- **103046-68-0**, 3,8-Diazabicyclo[3.2.1]octane, 3-benzyl-8-phenyl-, picrate **110553-68-9**, 2,5-Pyrrolidinedicarboximide, N-benzyl-1-phenyl- **111663-65-1**, 3,8-Diazabicyclo[3.2.1]octane, 3,8-dibenzyl-, dihydrochloride
(prepn. of)

RN 17740-41-9 CAPLUS

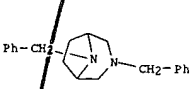
CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 3,8-bis(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 17740-42-0 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane, 3,8-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 35101-50-9 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane-2,4-dione, 8-benzoyl-3-(phenylmethyl)- (9CI) (CA INDEX NAME)

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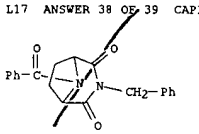
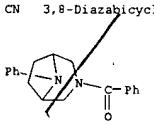


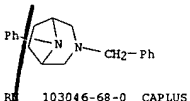
RN 102080-93-3 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane, 3-benzoyl-8-phenyl- (6CI) (CA INDEX NAME)



RN 102163-86-0 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane, 3-benzyl-8-phenyl- (6CI) (CA INDEX NAME)



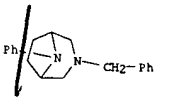
RN 103046-68-0 CAPLUS

CN 3,8-Diazabicyclo[3.2.1]octane, 3-benzyl-8-phenyl-, picrate (6CI) (CA INDEX NAME)

CM 1

CRN 102163-86-0

CMF C19 H22 N2



CM 2

CRN 88-89-1

CMF C6 H3 N3 O7

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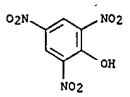
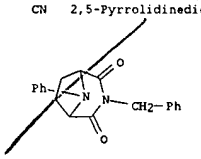
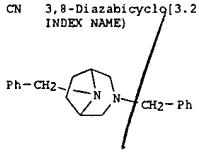


RN 110553-68-9 CAPLUS
CN 2,5-Pyrrolidinedicarboximide, N-benzyl-1-phenyl- (6CI) (CA INDEX NAME)



RN 111663-65-1 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane, 3,8-dibenzyl-, dihydrochloride (6CI) (CA INDEX NAME)



●2 HCl

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ACCESSION NUMBER: 1961:137533 CAPLUS
DOCUMENT NUMBER: 55:137533
ORIGINAL REFERENCE NO.: 55:25967i,25968a-i
TITLE: Bicyclic homologs of piperazine. I. Synthesis of 8-methyl-3,8-diazabicyclooctanes
AUTHOR(S): Cignarella, Giorgio; Nathansohn, Giangiacomo
CORPORATE SOURCE: Lepetit S.p.A., Milan
SOURCE: Journal of Organic Chemistry (1961), 26, 1500-4
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The synthesis and properties of 3-substituted 8-methyl-3,8-diazabicyclo[3.2.1]octanes (I), in which the 3-substituent was H, Me, Bu, Ph, and CH2Ph, were described. To a refluxed soln. of 500 g. di-Et meso-.alpha.,.alpha.-dibromoadipate (II) in 1500 ml. C6H6, 490 g. PhCH2NH2 (III) was added under stirring in 1 hr., the mixt. refluxed 24 hrs. while PhCH2NH2.HBr sepd., cooled, the ppt. filtered off, washed with C6H6, the C6H6 soln. evapd. in vacuo, and the oily residue distd. to give 350 g. cis-2,5-dicarbethoxy-N-benzylpyrrolidine (IV), b0.3 145-8.degree.; HCl salt m. 123-5.degree. (EtOH). A soln. of 60 g. IV in 600 ml. abs. EtOH was hydrogenated at 20 atm./40.degree. in the presence of 9 g. 10% Pd-C 2 hrs. to give 38 g. cis-2,5-dicarbethoxypyrrolidine (V), b0.3 95-6.degree.; HCl salt m. 134-5.degree. (EtOH-Et2O). A suspension of 200 g. V in 8 l. H2O refluxed under stirring 25-30 hrs. gave 98 g. cis-pyrrolidine-2,5-dicarboxylic acid (VI), m. 260-1.degree.. VI (67 g.) added to a 420 ml. 2N NaOH at -10.degree. was treated under stirring and cooling with 75 g. PhCH2OCOCl (VII) 30 min. and the mixt. stirred 2 hrs. at room temp. to yield 94 g. cis-N-carbobenzoxypyrrolidine-2,5-dicarboxylic acid (VIII), m. 125-7.degree. (H2O). VIII (79 g.) and 360 ml. Ac2O refluxed 1 hr. the solvent removed in vacuo and the residue kept at 140.degree./1 mm. 1 hr., 100 ml. anhyd. AcOEt added to the solid residue, the mixt. kept overnight at room temp., and the solid collected, washed with cold AcOEt, and dried yielded 58.1 g. (crude) N-carbobenzoxypyrrolidine-2,5-dicarboxylic acid anhydride (IX), m. 170-1.degree. (C6H6 or Me2CO). To 0.1 mole IX in 300 ml. anhyd. C6H6, 0.11 mole of appropriate amine in 50 ml. C6H6 was added with cooling, the mixt. heated on a water bath 20 min., and the solvent evapd. to give the crude ZN.CH(CONHR).CH2.CH2.CHCO2H (X) (Z = carbobenzoxy throughout; R = Me, Bu, Ph, CH2Ph) (Xa, Xb, Xc, and Xd, resp.). X (R = H), m. 179-81.degree., was obtained in 80% yield (a) by satg. with NH3 a C6H6 soln. of IX, evapg. the C6H6, dissolving the residue in H2O, and cautiously acidifying with 10% HCl; the oil sepd. solidified and crystd. from H2O to give 23.4 g. of the desired product; (b) by adding IX to 33% NH4OH to 0.degree., evapg. excess ammonia, and acidifying at pH 4 with 10% HCl. Xa-Xb refluxed with 5 vols. Ac2O 1-2 hrs., the solvent distd. and the residual oil kept 1-2 hrs. at 130-40.degree./1 mm., cooled, 200 ml. 1:1 Et2OC6H6 added, the insol. oil sepd., the clear soln. washed with 5% NaHCO3 and H2O, dried over Na2SO4, and the solvent evapd. gave the following CH2.CH2.CH.NZ.CH.CO.NR.CO (XI) (R, % yield from IX, b.p./mm. or m.p. and solvent of crystn. given): H, 50.4, 124-5.degree., MeOH; Me, 60, 170-2.degree./0.3; Bu, 63, 192-4.degree./0.3; Ph, 45, 148-9.degree., MeOH; CH2Ph, 64, 83-4.degree., MeOH. XI (R = Ph) was also obtained in 39.7% yield by adding a suspension of 20 g. IX in 60 ml. pyridine to BzN3 in 60 ml. pyridine; the mixt. was heated at 100-10.degree. 1 hr. till gas evolution subsided, the pyridine evapd. in vacuo, the residue taken up in

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ether, the solid collected, treated with a small amt. of H2O, and the undissolved product crystd. from MeOH. A soln. of 0.1 mole XI in 100 ml. anhyd. Et2O was added dropwise under stirring and cooling to a suspension of 0.5 mole LiAlH4 in 200 ml. Et2O, the mixt. refluxed 4-6 hrs., cooled to 0.degree. and cautiously decompd. with 50 ml. H2O, stirred 1 hr. at room temp., filtered, the inorg. matter washed with Et2O, the ether exts. collected, dried over Na2SO4 and the solvent evapd. gave I (R, % yield, b.p./mm., m.p. of dihydrochloride, methiodide, and dipicrate given): Me, 57, 50-2.degree./8, 260-2.degree., 290-2.degree., 242-5.degree.; Bu, 61, 54-5.degree./0.3, 245-7.degree., 218-20.degree., 220-2.degree.; Ph, 64, 104-5.degree./0.3 (m. 45-6.degree.), 180-2.degree., 262-4.degree., 172-4.degree. (monopicrate); PhCH2, 70, 88-90.degree./0.3, 213-15.degree., 250-1.degree., 228-30.degree.. A soln. of 5.4 g. I (R = CH2Ph) (XII) in 100 ml. abs. EtOH hydrogenated 2 hrs. at 50.degree. and 20 atm. in the presence of 1 g. 10% Pd-C gave 2.8 g. I (R = H) (XIII), b. 193-8.degree.; dihydrochloride m. 314-15.degree. (80% EtOH); methiodide (XIV) m. 224-5.degree.; dipicrate m. 247-50.degree.. XIV was obtained by mixing with cooling equimolar amounts of XIII (1 g.) and MeI (1.13 g.) in anhyd. Et2O and keeping 2 hrs. at room temp. The ether filtrate treated with excess MeI and kept overnight at 0.degree. gave I (R = Me) methiodide, m. 288-90.degree. (EtOH).
IT **96000-95-2**, 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-benzyl-2,4-dioxo-, benzyl ester
(prepn. of)
RN 96000-95-2 CAPLUS
CN 3,8-Diazabicyclo[3.2.1]octane-8-carboxylic acid, 3-benzyl-2,4-dioxo-, benzyl ester (6CI, 7CI) (CA INDEX NAME)